IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

THE CITY OF HUNTINGTON, Plaintiff, v. AMERISOURCEBERGEN DRUG CORPORATION, et al., Defendants.	:	Civil Action No. 3:17-cv-01362
CABELL COUNTY COMMISSION, Plaintiff, v. AMERISOURCEBERGEN DRUG CORPORATION, et al., Defendants.	:	Civil Action No. 3:17-cv-01665

BENCH TRIAL - VOLUME 26
BEFORE THE HONORABLE DAVID A. FABER, SENIOR STATUS JUDGE
UNITED STATES DISTRICT COURT
IN CHARLESTON, WEST VIRGINIA

JUNE 14, 2021

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PROCEEDINGS had before The Honorable David A. Faber, Senior Status Judge, United States District Court, Southern District of West Virginia, in Charleston, West Virginia, on June 14, 2021, at 9:00 a.m., as follows:

THE COURT: Do you have something?

MS. WICHT: Good morning, Your Honor. Just a very brief issue. It doesn't relate to Dr. Keyes, the witness who's on the stand. It relates to Ms. Keller who's the next witness up.

Your Honor, last night we received -- pursuant to the parties' agreement, we received the documents for Ms. Keller and we received the demonstratives as well.

We have raised an issue with the plaintiffs that the demonstratives for Ms. Keller contain opinions and analysis that is not in her report.

As to certain -- we're in the process of on-going discussions with the plaintiffs. And as to certain of them, we have resolved the issue. But there are other demonstratives that contain information that is not in Ms. Keller's report.

So, for example, she has a -- what Ms. Keller does, very briefly, is just look at prescribers within Cabell County. And she has a slide in her demonstratives, for example, where she compares that information to Queens, New

York, Honolulu, Hawaii, Hartford, Connecticut, nationwide. None of that analysis was in her report, Your Honor.

And there's one other -- that's slide 3. There's one other slide, slide 8, that has similar -- raises similar issues.

Our position is these are new analyses, new opinions. They weren't disclosed in her report. They were first disclosed at 11:00 p.m. last night and she shouldn't be allowed to present them today.

THE COURT: Do you want to respond, Mr. Ackerman?

MR. ACKERMAN: Yes. I've got a couple of responses, Your Honor.

The first one is that we assumed this would come up prior to Ms. Keller taking the stand. So Ms. Singer who is handling that testimony isn't here. But, regardless, we think the slides are wholly consistent with her report and I expect that Ms. Singer will be prepared to address that once she gets to court in order to take Ms. Keller's testimony.

MS. WICHT: And that's fine, Your Honor. I've been communicating with Ms. Singer this morning. I didn't realize that she wouldn't be in court right at this particular moment. That's fine.

I, I just would say that, then, I don't want to hear any complaints of sandbagging and now the witness is coming to the stand and you're trying to change what we're allowed

to do with her because we certainly raised it, you know, this morning and, and -- before court and in court this morning.

THE COURT: Well, I'm going to put this off until Ms. Singer is here. I received some good advice from one of my mentors years ago when I started practicing law. He said don't deal with all your problems today. You would be surprised how many of them just go away.

MS. WICHT: Good advice, Your Honor. Thank you.

THE COURT: All right. Do we have a witness? Is Mr. Hester ready to cross examine?

MR. HESTER: Yes, Your Honor. Thank you.

THE COURT: Good morning, Dr. Keyes.

THE WITNESS: Good morning.

THE COURT: You can resume the witness stand and, of course, you're still under oath.

KATHERINE KEYES, PLAINTIFFS' WITNESS, RESUMED THE WITNESS STAND

CROSS EXAMINATION

BY MR. HESTER:

Q. Good morning, Dr. Keyes.

A. Good morning.

Q. Dr. Keyes, you testified last week that there's a causal connection between exposure to opioids and opioid-related harm; correct?

A. Yes.

Q. And you testified that in your view, exposure is synonymous with supply; is that right?

A. I, I think there's multiple levels of exposure. And one level of exposure can be the supply of prescription opioids to a particular area. But individuals also are exposed to opioids when they personally are using them.

Q. And you remember Mr. Farrell asked you the question where he said, "Let's try to find another word that helps me understand. Is supply another word for exposure?" And you said, "Yes."

Do you remember that?

A. Yes. In that particular context, I think it was synonymous. But as a general matter, I wouldn't use those two words synonymously in all cases.

Q. So to be clear, when you talk about exposure or supply, you're talking about opioids that are out in the community and are being used or abused by individuals; correct?

A. I'm sorry. Can you repeat the question?

Q. Yes. So when you talk about exposure and supply, you're talking about opioids that are out in the community and are being used or abused by individuals; correct? That's the, that's the supply and the exposure you're focusing on; correct?

A. Yes.

Q. And with respect to prescription opioids in particular, that means the pills have either been dispensed by a pharmacy pursuant to a prescription or illegally trafficked or manufactured by criminals. It's one or the other. Correct?

A. The opioids that are in communities either arrived there through an illegal route or a legal route. So those would be the universe of ways that opioids could get into a community.

Q. And the source for the legal route, just to set the table -- I think we're on the same page. But to set the table, the source for the legal route would be dispensed by a pharmacy pursuant to a prescription written by a doctor; correct?

A. I would say in the majority of cases, you know, that that -- that would be true in a lot of, a lot of cases.

Q. And, and with respect to illegal opioids like heroin and illicit fentanyl, it means criminal traffickers or criminal actors have trafficked the drugs into the community and then sold them to end-users; correct?

A. That would be true for prescription opioids as well in many cases.

Q. Right.

A. So any, any way that the illegal route gets into the community, what -- regardless of what the opioid is, it

would be through a trafficking mechanism.

Q. Right. So your point is there may also be legal prescriptions that were issued at some point legally, but they've then been trafficked into a local area by drug traffickers; right?

A. That can occur.

Q. And, so, when you -- oh, when you opined last week that exposure to opioids causes harm, you mean that the ingestion of opioids into a person's body can cause harm; right?

A. There are other types of harms that are outlined in my report that can occur to communities when rates of opioid use are high; for example, to children and families.

Q. But those are ripple effects that begin with somebody ingesting opioids into their body; correct?

A. Yes.

Q. Now, you testified on Friday that it's very difficult to acquire opioid use disorder if you've never been exposed to opioids, almost a truism, right, if nobody -- if somebody has never used an opioid, they're unlikely to develop opioid use exposure; correct?

A. It would be impossible. It's a, it's a necessary cause of opioid use disorder.

Q. So, Dr. Keyes, I believe last week in your testimony you spoke about an over-supply of opioids; correct?

A. Yes.

Q. And you also mentioned that in your report. You talked about this idea that in your view, there was an over-supply of opioids in Cabell/Huntington; correct?

A. Yes.

Q. And you recognize, I take it, that there are legitimate medical needs for opioids; correct?

A. You know, as a, as a general matter, I think the legitimacy of opioids for any particular condition is one that has been controversial for a lot of different conditions.

Q. But you understand that opioids are a legitimate medicine that are used for legitimate purposes to treat pain; correct?

A. It would really depend on what the purpose is. There are many applications of opioids that have been argued were inappropriate.

Q. So you're not aware of any legitimate uses for opioids to treat pain?

A. Certainly, opioids relieve pain, and certainly there are circumstances in which an opioid would be an appropriate medication, particularly for end-of-life pain, for example, and some acute conditions for which opioids are prescribed for a short-term. But for a large majority of purposes for which opioids are prescribed, there's literature that has been developed calling into question their efficacy.

Q. Well, do you believe that when used as prescribed under medical supervision, opioid analgesics are effective and used as standard practice in managing pain?

A. I believe you're quoting the American Journal of Public Health article that I published in 2013. Right?

Q. You have a good memory.

A. Thank you very much. You know, I think that that sentence in that paper, the paper wasn't about the efficacy of opioids. And certainly in 2013 a lot of us had a broader view of opioids I guess I would say.

But the two citations I think that are, are made to that sentence, if you go to those citations, I think it provides a broader context for that particular sentence.

Q. Let me show you that document then.

A. Sure.

MR. HESTER: Your Honor, may I approach?

THE COURT: Yes.

BY MR. HESTER:

Q. You probably remember this one.

Dr. Keyes, I've handed you a document marked as Defendants' West Virginia Exhibit 2516. And the title is "Understanding the Rural-Urban Differences in Non-Medical Prescription Opioid Use and Abuse in the United States."

Do you see that?

A. Yes, I do.

Q. And this is an article you wrote; correct?

A. I was the first author, yes.

Q. So there were several authors, but you were one of the authors of this paper?

A. I was.

Q. And let me ask you to look at Page 3, and I'm using the small numbers in the left-hand corner. And I think we're together on this, but I just wanted to make sure the record is clear.

So there's -- under the heading "Self-medicating for Pain," there's a statement that says, "When used as prescribed under medical supervision, opioid analgesics are effective and used as standard practice in managing acute and chronic pain."

Do you see that?

A. I do.

Q. And that was a true statement at the time you wrote it; correct?

A. Well, I think I would just provide a little more context to that statement. I think -- if I were to write it today, I certainly -- and I think most epidemiologists would not have such a blanket statement about opioid prescribing certainly in 2013. I think many of us were affected by some of the same inappropriate marketing and misleading advertising and statements by industry that many doctors

were as well.

But I think if you actually go to the two references that I've cited there, what the underlying references suggest is that for a lot of purposes for which opioids were prescribed, although prescribing increased, there was very little evidence for efficacy.

So I think that that sentence is inartfully worded I would say. And if I were to write it again today, I would certainly provide a lot more context that would be consistent with the actual science that is cited in those underlying citations.

MR. HESTER: Your Honor, I would move to strike the answer as not responsive. I asked Dr. Keyes whether it was accurate at the time she wrote it, and she's now answered a different question.

THE COURT: Well, I'll grant the motion to strike. You need to answer the precise question, Dr. Keyes.

MR. FARRELL: Judge, I'd like to at least --

THE COURT: Mr. Farrell.

MR. FARRELL: Yes, sir. I'd like to say that I oppose his motion to strike and note it for the record, please.

THE COURT: Well, she can explain her answer and -- but I believe she went a little beyond that. So your objection is noted, Mr. Farrell.

MR. FARRELL: Thank you.

BY MR. HESTER:

Q. So, Dr. Keyes, I just wanted to clarify that at the time you wrote this, you believed this to be a true statement; correct?

A. At the time that I wrote that, I, I -- yes, I believed it to be -- I believed it to be a statement that was based in the literature.

Q. And you have not undertaken to determine the supply of opioids that are needed to meet medical needs in West Virginia, have you?

A. I believe that that type of information is in my report.

MR. HESTER: Let me pull up, please, Dr. Keyes' deposition from this case at pages -- at Page 126, lines 6 to 10.

BY MR. HESTER:

Q. Dr. Keyes, first let me ask you, do you remember being deposed in this litigation?

MR. FARRELL: Objection, Your Honor. I'm not quite sure that impeachment has been established at this point in time.

THE COURT: Well, we don't know yet.

MR. FARRELL: So before we put up transcripts of other proceedings, I think the foundation has not yet been

laid to bring up her prior testimony.

MR. HESTER: Your Honor, I asked her a question and, and now I have a deposition excerpt that I believe the response is the same question that she answered during her deposition.

THE COURT: Mr. Ackerman.

MR. ACKERMAN: Yeah, but the problem is that counsel hasn't established that yet. He asked a question and then went straight to the deposition which is not the proper method of establishing --

THE COURT: Well, you got an answer from her, didn't you, Mr. Hester?

MR. HESTER: I did get an answer.

THE COURT: Overruled. Go ahead.

BY MR. HESTER:

Q. So, Dr. Keyes, you recall being deposed in this litigation; correct?

A. I do.

Q. And you and I had the pleasure of going through that deposition; correct?

A. Yes.

Q. And, so, let me ask you to look at Page 126, line 6.

And, so, my question to you was, "So you've not untaken any evaluation of how many pills are needed in Cabell/Huntington?" That was my question.

And your answer was, "I -- no, I have not taken -- I've not undertaken that."

Do you see that?

MR. ACKERMAN: Your Honor, I want to voice an objection because the question on this deposition is different than the question that was asked of the witness. And that's exactly why we need to establish foundation before we bring up other testimony.

THE COURT: Well, I think it's close enough and I'll overrule the objection.

Go ahead, Mr. Hester.

BY MR. HESTER:

Q. And your answer was, "I have not taken -- I have not undertaken that." Do you see that?

A. I do.

Q. And was that a correct statement when you gave it?

A. No, I, I have not -- myself have not undertaken any statistical evaluation. I have reviewed the literature which is what is in the report.

Q. But my question to you in that deposition was you have not undertaken any evaluation of how many pills are needed in Cabell County. And your answer was, "No, I have not undertaken that."

Is that correct when you said it?

A. That's what the deposition says. I think my

interpretation of the question was whether I had undertaken a statistical evaluation.

Q. Well, Dr. Keyes, I'm asking was your testimony accurate when you gave it in your deposition?

A. Yes. I have not undertaken a statistical evaluation, although I have reviewed the literature. So I just want to, I guess, clarify my interpretation of the question.

Q. And you have not undertaken any analysis of the pain needs specifically in Cabell/Huntington, have you?

A. No, I have not.

Q. So you don't know the level of supply needed to meet the pain needs of Cabell/Huntington; correct?

A. I would say that the, the consensus of the literature that I cite in the report is that in terms of the opioid needs in the community, the pre-opioid epidemic levels were the levels that should be considered as, as meeting the pain needs of the community.

MR. HESTER: Your Honor, I move to strike as nonresponsive.

THE COURT: I grant the motion to strike. Go ahead.

BY MR. HESTER:

Q. So, Dr. Keyes, you do not know the level of supply of prescription opioids needed to meet the pain needs of Cabell/Huntington; correct?

A. The -- I, I do know. I have an opinion about that.

Q. Well, you've not undertaken any analysis for the pain needs in Cabell/Huntington; correct? You just said that.

A. Correct.

Q. And, so, you don't know the level of supply of need to meet those pain needs because you don't know the level of pain needs in the community; correct?

A. Again, I could point to literature to inform the answer to that question.

Q. But you haven't undertaken that analysis of pain needs in Cabell/Huntington; correct?

A. That's right.

Q. Now, Dr. Keyes, you prepared a 54-page, single-spaced report in this case; right?

A. I, I trust that that's correct.

Q. I think that's the right count. In small font too I would add; correct?

A. I suppose it was small.

Q. You did not evaluate any specific distributors in your report; correct?

A. The information that is included in the report includes aggregated data across distributors, although I did not evaluate any specific company by name.

Q. And your report does not mention McKesson, Cardinal, or ABDC at all, does it?

A. It does not.

Q. And you did not review any documents relating to the distributors' individual activities, did you?

A. I, I don't believe -- I'm just trying to remember what is included in the ARCOS data. I'm not sure -- I do believe there's some information on specific distributors, although the information in my report is in the aggregate.

Q. Dr. Keyes, I was asking about documents. You did not review any documents relating to the distributors' individual activities, did you?

A. I believe I reviewed some documents about market share generally.

MR. HESTER: May we bring up Dr. Keyes' deposition, please, from this case, Page 301.

BY MR. HESTER:

Q. And, Dr. Keys, again, you recall being deposed in this case; correct?

A. I do.

Q. Let me ask you to look at Page 301, line 1.

My question to you was, "But you've not reviewed specific documents relating -- related to their individual activities?"

Do you see that question?

MR. FARRELL: Objection, Your Honor. So, again, his first question is materially different than the question

on the screen. So I would object to the first question as being vague. And I would object to the use of the transcript as being improper impeachment.

THE COURT: Overruled.

Go ahead, Mr. Hester.

BY MR. HESTER:

Q. So my question was, "But you've not reviewed specific documents related to their individual activities?"

Do you see that question?

A. I do.

Q. And your answer was, "Generally, no." Was that your answer?

A. That's what's written.

Q. Well, and is that what you answered, Dr. Keyes?

A. That's what I answered in the deposition.

Q. And was that answer true and correct when you gave it?

A. Yes. As I've said, as I'm thinking it over, you know, I did see some documents related to market share. So I think the "generally, no" statement leaves some room for, yes, I have seen some documents related to market share.

Q. You did not assess any individual distributor's contribution to opioid supply relative to other distributors; correct?

A. I have not.

Q. And as part of your methodology, you did not evaluate how many opioids that McKesson, Cardinal, or ABDC individually had shipped into Huntington and Cabell County; correct?

A. That's correct.

Q. Your report, in fact, does not make any mention as to how many opioids McKesson, Cardinal, or ABDC individually shipped into Huntington or Cabell County; correct?

A. That's right. It's the total number of shipments.

Q. And you don't know the respective market shares of McKesson, ABDC, and Cardinal vis-à-vis their distributions into Cabell and Huntington; correct?

A. As I mentioned, I have reviewed documents related to that, although that's not my area and it is not in my report.

Q. And you don't know what their respective market shares are for their distribution of opioids into Cabell and Huntington County; correct?

A. Not off the top of my head.

Q. I'm sorry, Cabell County and Huntington. Sorry. You don't --

A. Not sitting here today.

Q. And you don't have any knowledge in relation to the operations of McKesson, Cardinal, or ABDC in Cabell County and Huntington; correct?

A. Can you clarify what you mean by knowledge?

Q. Do you have any knowledge in relation to the operations specifically of McKesson, ABDC, or Cardinal in Cabell County and Huntington?

MR. ACKERMAN: Objection, vague.

THE COURT: Overruled.

THE WITNESS: I'm, I'm generally familiar with the activities of distributors, but I have not reviewed any specific material related to operations in Cabell and Huntington that have -- that were in my report or that informed the opinions that I've given in the report.

BY MR. HESTER:

Q. So you didn't discuss those factors in your report; correct?

A. That's -- well, I'm sorry. Can you -- the question is the --

Q. Do you have any knowledge in relation to the operations of McKesson, Cardinal, or ABDC specifically in Cabell County and Huntington?

A. In the report I discussed general distribution operations, but not with regard to any company specifically.

Q. And, so, your answer is "no;" correct?

A. Correct.

Q. You did not review the content of any distributor Suspicious Order Monitoring Program for purposes of your

report in this case; correct?
A. That's correct.
Q. You did not review any of the orders that were made by pharmacies in Huntington or Cabell County for prescription opioids; correct?
A. No, I did not review any specific orders.
Q. And you're not offering an opinion on how many opioids McKesson, Cardinal, or ABDC shipped to any specific pharmacy in Huntington or Cabell County; correct?
A. Not a specific pharmacy, no.
Q. And you cannot identify a single prescription opioid that was distributed by the defendants in Cabell County or Huntington that in your opinion should have been investigated and not shipped? That's not something you've done; correct?
A. That's not in, in the lens of epidemiology. We typically don't look at individual prescriptions.
Q. And you're not aware of any occasion where McKesson, ABDC, or Cardinal shipped opioids that exceeded their permissible quotas set by the DEA; correct?
A. I have not looked at specific quota levels and shipments that have exceeded them.
Q. You're not aware of any evidence that McKesson, Cardinal, or ABDC shipped pills into Huntington or Cabell County that exceeded the levels doctors had prescribed;

correct?

A. I, I have not reviewed evidence related to specific shipments.

Q. And, so, you're not aware of any evidence that they shipped pills into Huntington or Cabell County that exceeded the levels prescribed by doctors; correct?

A. Right. That is not something in my report.

Q. You've published, I believe you said last week, 306 peer-reviewed articles; is that correct?

A. Yes.

Q. And about 35 to 40 of those relate specifically to opioid use and opioid harms; is that correct?

A. Yes.

Q. And some of them address the causes of the opioid crisis; right?

A. That's right.

Q. None of your articles that you've written on the opioid crisis or opioid harms refer to McKesson as a cause of the opioid crisis; correct?

A. It refers to over-supply and distribution more generally.

Q. Can you answer --

A. I have not named McKesson in any of those articles.

Q. So none of your articles refer to McKesson as a cause of the opioid crisis; correct?

A. In the sense that McKesson is a distributor and the distribution of opioids are identified as a cause, I think it's fair to say that I have identified McKesson.

MR. HESTER: Your Honor, I move to strike as not responsive.

THE COURT: Well, I'll overrule that. I think that was responsive.

BY MR. HESTER:

Q. None of your articles refers to distributors collectively as a cause of the opioid crisis; correct?

A. No, that's incorrect. I talk about the over-supply of prescription opioids.

Q. I'm talking about distributors collectively. I'm not talking about over-supply. My question is none of your articles refers to distributors collectively as a cause of the opioid crisis; correct?

MR. ACKERMAN: Objection, asked and answered.

THE COURT: Overruled.

THE WITNESS: I do talk about distribution of opioids as a cause of the opioid crisis. And, therefore, the contributors to distribution would be the cause of the distribution. It doesn't arise magically.

MR. HESTER: Let me ask to pull up the *Frye* transcript from New York, Page 153.

BY MR. HESTER:

Q. Dr. Keyes, do you remember testifying in a *Frye* hearing in New York?

A. I do.

Q. I believe you mentioned that last week; correct?

A. Yes.

Q. And let me show you Page 153 of the transcript, line 17.

And there was a question asked, "Is there a publication you can point us to where you say that in that publication that distributors as a class caused the opioid crisis?"

And your answer was, "Not back then, no."

Do you see that?

MR. ACKERMAN: Objection, Your Honor. This isn't the same question that was asked. Frankly, if you look at the immediate preceding question on this transcript, it has the exact same answer that the witness just gave. This is improper impeachment, Your Honor.

MR. HESTER: I object to the speaking objection, Your Honor. If the objection is improper impeachment, that should be the objection.

THE COURT: Well, I'm going to overrule the objection.

You can go ahead, Mr. Hester.

BY MR. HESTER:

Q. Was that, was that answer that you gave, Dr. Keyes,

accurate and true when you gave it?

A. This is a different question.

Q. I'm asking whether the answer that you gave to the question on the transcript was true and accurate when you gave it.

A. Yes.

Q. All right. Dr. Keyes, let's talk about a few of your articles in a little more detail.

MR. HESTER: May I approach, Your Honor?

THE COURT: Yes.

BY MR. HESTER:

Q. Dr. Keyes, I've handed you a document marked as MC-WV-01806. And on its face it appears to be an article, "A Critical Review of the Social and Behavioral Contributions to the Overdose Epidemic."

Dr. Keyes, I take it you're familiar with this article?

A. I am.

Q. And you're one of the authors of it; correct?

A. Yes.

Q. And if you look at Page 12 and, again, working off of the small numbers at the bottom, and this is under the heading for "Author Contributions" there's a statement, "K.M.K. provided feedback on the initial structure of the paper, wrote sections, and critically reviewed and edited multiple versions of the manuscript."

Do you see that?

A. I do.

Q. And I take it K.M.K. is a reference to you?

A. Yes.

Q. So that's a fair description of what you did in relation to this article?

A. Yes.

Q. So this article was originally published as a review in advance on November 30, 2020; correct?

A. Yes.

Q. And then it was published in its final form in the Annual Review of Public Health in April, 2021; is that correct?

A. Yes.

Q. And, so, it was published after you had been retained as an expert in this case; correct?

A. Yes.

Q. And it was published after you wrote your expert report; correct?

A. The expert report for --

Q. For this litigation.

A. Yes.

Q. And it was published after you sat for your deposition in this case; correct?

A. I don't remember the exact timing, but I trust that --

Q. I think it was September of last year that we had the pleasure. Does that sound about right?

A. That sounds right.

Q. So this paper went through a process of peer-review; is that correct?

A. Yes.

Q. And what does peer-review mean? Can you explain just very briefly what peer-review means?

A. Sure. When you submit a journal -- an article to a journal, the editor of the journal will decide whether it merits further consideration. And if it does, they will invite, you know, other scientists who have expertise in this area to read the paper and say whether it has scientific merit.

Q. And, so, there, there are peers that provide input on the article. And then that peer-review process ensures the legitimacy or the accuracy of the article? Is that the concept?

A. Well, I wouldn't say that it ensures accuracy or legitimacy. It's really more of, you know, having your peers read the paper and, and provide an assessment to the editor really of whether the paper is, is scientifically meritorious of publication.

Q. And is it a fair statement that peer-review is a meaningful step in publishing an article, that that means

something about the, the, the article?

A. It's certainly a requirement of most journals that an article is, is identified as meritorious by your scientific peers.

Q. And if the peers were to say that it was not meritorious or lacked weight or had problems, would that cause the article either to be changed or not published?

A. Ultimately, the decision rests with the editor. Certainly, editors listen to the feedback of peer-reviewers. And, so, if your peers -- if the peer-reviewers all said, you know, this article is not scientifically meritorious, then an editor would likely not accept the paper in the journal.

Q. So let me ask you to look at Page 3 of this article, please. And, again, I'm working off of the small numbers at the bottom left.

I wanted to focus you under the heading for "Supply Drivers of the Opioid -- of the Overdose Epidemic." And then there's a subheading for "The Prescription Opioid Supply: Chronic Pain and Opioid Prescribing."

Do you see that?

A. I do.

Q. And there's a first sentence under that heading that reads, "The supply-side roots of the overdose epidemic in the United States lie at the intersection of two social and

behavioral forces that, together, led to the proliferation of opioid prescribing in the 1990s, especially for non-cancer acute and chronic pain conditions."

Do you see that?

A. I do.

Q. Is that a true statement?

A. I believe that's an accurate representation of the literature.

Q. And it goes on to say, "The first force was a shift in treatment approaches for chronic non-cancer pain, including a campaign by professional pain societies and the U.S. Joint Commission, the nation's largest accrediting body for healthcare organizations, to consider pain as the fifth vital sign and to improve the quality of care for chronic pain."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. I think that that accurately represents the literature.

Q. Then let me point you to the next paragraph which begins, "The second related force involved the pharmaceutical industry's concerted efforts to advocate for the long-term use of opioids as a safe, non-addictive, effective, and humane alternative to treat non-cancer pain."

Do you see that?

A. I do.

Q. And then it goes on a few sentences later to say, "In 1996-2002, Purdue Pharma provided funds for educational campaigns supporting the use of opioids to treat chronic non-cancer pain and supported efforts by pain professional societies, the U.S. Joint Commission, and the Federation of State Medical Boards to advocate for the use of opioids to treat pain."

Do you see that?

A. Yes.

Q. And is that a true statement?

A. I believe it reflects the literature.

Q. Let me point you to Page 4, please. Just before the heading for the illegal opioid supply, there's a statement, "The expansion of PO supply --" and I take it PO means prescription opioids; right?

A. That's right.

Q. "The expansion of PO supply increased opioid-related harm through several pathways affecting both individuals who initially used opioids as prescribed but developed impaired control over use and individuals who used non-medically and obtained opioid prescriptions through family, friends, or an illicit diversion source."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. It reflects the literature, yes.

Q. And, so, in this sentence, there's a reference to using opioids non-medically. And that means opioids not being used pursuant to a doctor's correction [sic]; correct? I'm sorry. Doctor's direction; correct?

A. Yes.

Q. And, for instance, using opioids without a prescription is a form of non-medical use; correct?

A. That's right.

Q. Stealing opioids from somebody's medicine cabinet and then ingesting them is a form of non-medical use; correct?

A. It is.

Q. Buying opioids from a drug trafficker and ingesting them is a form of non-medical use; correct?

A. Yes.

Q. Also, taking pills more frequently or for a longer period of time than prescribed is also a form of non-medical use; correct?

A. That's right.

Q. The reference here to -- in this sentence we're looking at just before the next paragraph where it says that opioids were obtained through family or friends, is that -- I take it the reference there means someone had a legitimate prescription and then gave or sold them to family or

friends; correct?

A. Not necessarily. I mean, a lot of people can obtain prescription opioids through non-medical sources and give them to family or friends or sell them to family or friends as well.

Q. Well, I wanted to ask about the idea that individuals who used non-medically obtained opioid prescriptions through family or friends. And, so, is the point there that the family or friends may have had a legitimate prescription and then gave those pills or sold them to someone else who used it non-medically?

A. That could happen. Certainly, one source of opioids is a family or friend who received a prescription for opioids and didn't finish the bottle or, you know -- but, also, the family or friend could have themselves obtained the prescription opioids non-medically.

So the literature that forms the basis of that statement usually asks people, "Where do you obtain your opioids?" And people say family or friends, but they don't specify where the family or friend got the medication.

Q. So your point is there might be one set of circumstances where a family member had a prescription but didn't use all the opioids and then either gave or sold them to somebody else. That's one scenario; correct?

A. That is one scenario.

Q. And another scenario might be that a family member him or herself had obtained opioids illegitimately and then handed them over to somebody else; correct?

A. Yes. And I think a third scenario is that people obtain opioids from a medical source where the prescriber is not prescribing for a legitimate medical need for example.

Q. So there's a reference in that same sentence we were just looking at to individuals who used non-medically and obtained opioid prescriptions from an illicit diversion source. Do you see that?

A. Yes.

Q. And does the reference to an illicit diversion source mean some sort of drug trafficker or someone who's selling the opioids?

A. That's one possibility for an illicit diversion source.

Q. But this is diversion after the prescriptions have -- I'm sorry. Let me strike that and start over. This is not diversion in the closed system for controlled substances; correct?

A. The definition of diversion that I used, just to -- if I could answer your question with a little bit of context, I hope that's okay.

The definition of diversion that I use in the report is any opioids that are used by someone who they were not prescribed for. So an illicit diversion source would

include any use of opioids by someone who they were not prescribed for which would include opioids that arrived through the closed system.

Q. But it could -- but the point would be when you're talking here about an illicit diversion source, you're talking about an illicit diversion source after the pills are outside of a pharmacy; correct?

A. Again, I, I don't know how -- exactly how to answer that because the diversion definition is the use of an opioid by someone for whom it is not prescribed.

So an illicit diversion source would be any source that got a prescription to someone for whom it is not prescribed. And that would include a number of different mechanisms, including a bottle that left the pharmacy and got into the hands of someone it wasn't prescribed for. But it would also include a lot of other potential diversion mechanisms.

Q. A very common one that you've seen and you discuss in your report is the scenario where the pills are prescribed to somebody. They're -- it's a legitimate prescription. But then they later end up into illicit channels. Correct? That's a very common pattern you've seen?

A. There is a common pattern whereby people have unused medication from an opioid prescription. I would say that is common. But there are other mechanisms as well.

Q. Let me ask you to look at Page 2, please.

In the middle of the second paragraph there's a statement, "Heroin use and related harms increased in the mid 2000s surpassing prescription opioids as a cause of opioid-related overdoses in 2015."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. Yes, based on the CDC data.

Q. And then let me ask you to look at Page 4 again.

There's -- about three sentences in under illegal opioid supply, in that paragraph there's a sentence that reads, "While state restrictions on prescription opioids may have increased the risks of transition to heroin use among people with a dependence on prescription opioids, shifts in the heroin market also likely played an important role."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. Yes, based on the literature.

Q. In that same paragraph it says, it says, "In the mid 1990s the U.S. supply of South American heroin increased substantially while the fraction of the market controlled by the Asian heroin decreased dramatically."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. That's my understanding of the literature.

Q. And then it goes on to say, "Mexican black tar heroin dominated the West Coast market while Colombian heroin dominated the East Coast."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. Again, that's my understanding of the literature.

Q. And the reference to Colombian heroin there, that's to a white powder heroin; correct?

A. Yes.

Q. And then it goes on to say, "Abundant supply, low price, and high purity of the Colombian heroin reduced the price per gram of pure heroin."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. Based on my read of the literature.

Q. And then it goes on to say, "In 2013 the illegal opioid market shifted again with the introduction of fentanyl, often mixed with heroin or sold as counterfeit oxycodone and benzodiazepines."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. That's my understanding of the literature.

Q. It goes on to say that, "Fentanyl is cheaper to produce. The wholesale price is one-tenth of heroin's price by weight, and is 30 to 40 times stronger than heroin, so that a comparable dose would be 1/300 to 1/400 of the wholesale price of heroin."

Do you see that?

A. Yes.

Q. And that's a true statement; correct?

A. Based on my read of the literature.

Q. There's a reference here to counterfeit oxycodone. Do you see that?

A. Oh, yes.

Q. And that reference means fentanyl being sold as a counterfeit prescription opioid perhaps mixed with some filler; correct?

A. Can you say that question again?

Q. Yeah, sorry. I didn't ask that very well. When it refers to counterfeit oxycodone, that's referring to a counterfeit prescription pill; correct?

A. Yes.

Q. And the counterfeiting is done by the drug dealer; is that correct?

A. My -- that's my understanding. They are manufactured

outside of the pharmaceutical company.

Q. And the counterfeit pill typically includes some fentanyl; is that correct?

A. It could. That's what that sentence is saying.

Q. And, and presumably it wouldn't be a full-size pill all of fentanyl. It would have some filler or something else as part of the counterfeit?

A. It's possible.

Q. If it were a full-size pill with fentanyl, it would kill somebody almost immediately; correct?

A. It would depend on the amount of fentanyl and the tolerance of the individual taking it.

Q. If you look back at Page 2 again, again in that top section under "National Trends," there's a statement that says, "Overdoses involving synthetic opioids other than methadone became the predominant opioid cause of death."

Do you see that?

A. Yes.

Q. And that's a true statement; correct?

A. Yes, that is what the data show.

Q. And synthetic opioids there as it's used is referring primarily to illicit fentanyl; correct?

A. In terms of what's causing the increase in overdoses?

Q. Yes.

A. Yes, that is what the consensus is.

Q. It could also be referring to carfentanil; correct?

A. Yes.

Q. And you're aware that both illicit fentanyl and carfentanil are much more potent than heroin; correct?

A. Yes.

Q. In that -- in the next paragraph it says, "Overdose deaths involving stimulants such as cocaine and methamphetamine began to increase rapidly in 2015 due in large part to adulteration of those substances with synthetic opioids."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. That's what the literature shows.

Q. And when it says "adulteration" there, that's referring to something that's being done by the drug dealer to cut the heroin or to create a counterfeit tablet; correct?

A. Yes.

Q. And, so, when that occurs -- when, when the heroin is being cut or a pill is being counterfeited, the drug dealers are, are in effect cheating the user by adulterating the heroin with fentanyl; correct?

A. They're -- I'm sorry. They're cheating the user?

Q. Cheating the user because they're not giving the user -- if the user thinks he or she is buying heroin and

they get heroin adulterated with fentanyl, that's not what the user expects; right?

A. It would really depend on the, on the particular user and the drug market. There are some drug users who prefer fentanyl.

Q. You're aware that many drug users who are taking heroin are unaware that the heroin has been adulterated with fentanyl; correct?

A. There are many users who are unaware. But there are users who, who prefer the potency of a strong opioid.

Q. But for the users who are unaware that heroin is being cut with fentanyl, they may experience an overdose without knowing the risk they were taking because they weren't aware that the heroin had been cut with fentanyl; correct?

A. If -- I mean, that's -- it's sort of tautological. If the user is unaware, then the user would not know that there is fentanyl by definition of being unaware. And what I'm saying is that many users are aware.

Q. But the user who is unaware would also, therefore, not know the risk that he or she is taking by ingesting heroin that's been adulterated with fentanyl; correct?

A. I would say any user who's not aware of the potency of the drugs that they're taking is taking a risk.

MR. FARRELL: Excuse me, Mr. Hester. I got lost there. Can you tell me the page number?

MR. HESTER: Sorry, Paul. It was Page 2.

MR. FARRELL: I'm sorry. I missed it.

BY MR. HESTER:

Q. All right, Dr. Keyes, you can put that one aside for now. We'll look at another one.

MR. HESTER: May I approach, Your Honor?

THE COURT: Yes.

BY MR. HESTER:

Q. Dr. Keyes, we've handed you what's been marked as Defendants' West Virginia Exhibit 2518. On its face it has a heading "Prescription Opioid Use Disorder and Heroin Use Among Youth Non-Medical Prescription Opioid Users from 2002 to 2014."

Do you see that?

A. I do.

Q. And I take it this is an article that -- for which you were one of the co-authors; correct?

A. Yes.

Q. And it was published in February of 2017?

A. Yes.

Q. And in this article you set forth causes of the increasing trend in prescription opioid use disorder that had been observed in young adults at that time; is that correct?

A. This article -- there's no abstract that is produced

with this. I'm not sure if that can be provided as well. But this article examined changes in prevalence of heroin use among non-medical prescription opioid users. I don't believe it assessed risk factors or provided a causal analysis.

Q. Let me look with you at Page 7 of the article. Again, we're using the small numbers on the left.

There's a -- this is a paragraph that begins, "Although our study does not assess underlying causes, the increasing trend in prescription opioid use disorder observed in young adults might be at least partially explained by historical factors described elsewhere in the literature."

Do you see that?

A. I do.

Q. And, so, what -- when you're referring to the literature there -- I think I've learned over time this is one of the things epidemiologists do is they study literature and draw conclusions from it; correct?

A. Yes.

Q. And that's what you're doing here. You're summarizing a body of literature by referring back to it; correct?

A. I don't think this summarizes the totality of the literature. I think this points to a number of underlying potential explanations, but it doesn't assess or review the literature for the validity of those explanations.

Q. But it did pull out propositions that had been found in the literature I take it; correct?

A. Right. This is typically what's done in kind of discussion sections as we look to the body of literature and we say, okay, what are the potential explanations for the trends that we're seeing and what research program would we need to initiate in order to provide the kind of causal analysis on those factors that I think you're suggesting.

Q. So when you refer here to the historical factors described elsewhere in the literature, you're referring to other papers that had previously identified these various factors that are discussed as ones that might be contributing to prescription opioid use disorder; correct?

A. Yes.

Q. And, so, the first factor that's listed is a shift in medical practice of prescribing opioids from end-of-life pain and cancer to chronic non-cancer pain, particularly in non-adults [sic]. Do you see that?

A. In young adults I think.

Q. I'm sorry, young adults.

A. Young adults.

Q. So do you see that statement?

A. I do.

Q. And this is a factor that you believe contributed to increases in opioid use disorder in West Virginia?

A. Yes.

Q. And next -- the next factor that's referred to is an increased rate of opioid prescription by physicians due to a higher sensitivity to patient's pain. Do you see that?

A. I do.

Q. And that's a factor that you believe contributed to increases in opioid use disorder in West Virginia; correct?

A. Yes.

Q. Next is the -- a reference to the endorsement of pain as a fifth vital sign by the Joint Commission with a controverted pain metric. Do you see that?

A. I do.

Q. And that's a factor that you believe contributed to opioid use disorder in West Virginia; correct?

A. Yes.

Q. And then further down it states, "State lobbying by pain advocates for prescription opioid use." Do you see that?

A. I do. You skipped one. I don't know if you want to go over that one.

Q. I don't think so, but -- I think that's the next one I wanted to ask you about. And that's a factor that you believe -- the reference I wanted to point you to is state lobbying by pain advocates for prescription opioid use. Do you see that?

A. I do.

Q. And that's a factor that you believe contributed to increases in opioid use disorder in West Virginia; correct?

A. Yes.

Q. The next one I wanted to ask you about is physician sensitivity to pain exploitation by opioid users. Do you see that?

A. Yes.

Q. And that's referring to doctor sensitivity to patients who overstate their medical need for opioids in order to obtain a medication; correct?

A. That is possible.

Q. And that's a factor that you believe contributed to increases in opioid use disorder in West Virginia; correct?

A. Yes.

Q. The next reference is doctor shopping by patients. Do you see that?

A. I do.

Q. And that's a factor that you believe contributed to increases in opioid use disorder in West Virginia?

A. Yes.

Q. The next is overprescribing which leaves excess medications available for misuse or redistribution via non-medical sanctioned venues. Do you see that?

A. Yes.

Q. And that's a factor that you believe contributed to increases in opioid use disorder in West Virginia; correct?

A. That's right.

Q. You don't mention the conduct of wholesale distributors like the defendants anywhere in this article; correct?

A. I believe that would be included in the one that you skipped.

Q. Which one are you referring to?

A. Increased distribution of opioids by the pharmaceutical industry in creation of an opioid-rich environment.

Q. And the pharmaceutical industry had secured approval for various opioids; correct?

A. They had.

Q. And the pharmaceutical industry had secured approval from the FDA to sell opioids based on representations about the risks and benefits of those opioids; correct?

A. The opioids were approved by the FDA, yes.

Q. And the pharmaceutical industry that had developed those for manufacturers who applied for approval from the FDA for those drugs; correct?

A. I'm sorry. Can you say that sentence again? I didn't understand the question.

Q. Yes. The, the pharmaceutical manufacturers were the ones who applied to the FDA for approval for drugs based on representations about the risks and benefits of those drugs;

correct?

A. The manufacturers applied to the FDA, yes.

Q. Let's go to another article that you also wrote. I'm sorry. We already have this one. I've already given you this one, Dr. Keyes. It's the one I've handed you previously, Defendant's Exhibit 2516, "Understanding the Rural-Urban Differences in Non-Medical Prescription Opioid Use and Abuse in the United States."

And I think we talked about this. You wrote this article, correct, along with others?

A. I was a co-author, yes.

Q. And this article specifically discusses West Virginia; correct?

A. Yes.

Q. And this is the article that you -- let me back up. You mentioned in your testimony last week that Mr. Farrell first contacted you after reading an article you had written. This is the article; correct?

A. That is what he told me.

Q. I'd like to direct your attention to Page 3 of the article, again using the small numbers on the left.

Actually, we've already discussed -- well, I'm going to go to another place in this page.

The bottom of the left-hand column, "States with large rural populations such as West Virginia are among the

highest prescribers of opioid analgesics."

Do you see that?

A. I do.

Q. And that's a true statement; correct?

A. Yes.

Q. And beginning on Page 3, you identify a number of factors that may explain the high rate of opioid prescribing places like West Virginia; correct?

A. Well, the article is really about explaining urban-rural differences, not just overall prescribing levels.

Q. But let me point you to the paragraph I'm thinking of. In the middle column there's a second paragraph that begins "rural populations." That's the paragraph I wanted to ask you about.

A. Okay.

Q. And that's a paragraph where you're talking about some of the factors that may lead to higher levels of opioid prescribing in rural populations; correct?

A. Yes.

Q. And, so, one point you make in that paragraph is rural populations are on average older and, thus, there may be more chronic pain for which management with opioid analgesics is indicated.

Do you see that?

A. I do.
Q. And that's a true statement; correct?
A. Yes, within the context of all the other factors that I'm talking about in the article. But that is one factor that could lead to increases in prescribing.
Q. In rural areas?
A. In rural areas.
Q. Then it goes on to say, "Chronic pain and injury are more common in rural than in urban areas."
Do you see that?
A. I do.
Q. And that's a true statement; correct?
A. That was my read of the literature when I was writing this article.
Q. And you based this article that you wrote in 2014 on the literature you had reviewed; correct?
A. Yes, at that point.
Q. And then there's another statement, "Prescription narcotics are often prescribed to maintain a steady work flow in mines and other heavy labor occupations."
Do you see that?
A. That was -- the first part of the sentence specifically referred to Kentucky. But, yes, that's what the sentence says.
Q. But it's referring to rural areas such as Appalachian

Kentucky; right?

A. Yes.

Q. And, and I take it that that same observation would apply to rural areas in Appalachian West Virginia; correct?

A. The specific, you know -- Jennifer Havens, who is a co-author of the article, that's her particular area of interest is Appalachian Kentucky. And, so, I haven't reviewed the literature on whether that generalizes to Appalachian West Virginia.

Q. So you don't know whether observations about the nature of pain needs in Appalachian Kentucky would be comparable to needs in Appalachian West Virginia? You don't know?

A. I haven't reviewed that literature, so I wouldn't want to offer an opinion on that.

Q. Okay. So, so here it's talking about Appalachian Kentucky. By the way, you understand that in Appalachian West Virginia there is a -- there's a heavy work flow in mines and other heavy labor occupations; correct?

A. I'm generally familiar with the labor industries that are in West Virginia.

Q. And you understand there's a lot of heavy physical labor expected of the people of West Virginia; correct?

A. I would say in those particular industries, they are physically laborious.

Q. And, for instance, mining is an important industry in

West Virginia; correct?

A. I would not offer an opinion on the importance of any one industry. I'm an epidemiologist, so I review the data on what the occupations are.

Q. Do you have an understanding, though, that, that there is a need for prescription opioids -- well, maybe -- let me back up. Let me ask it a different way.

Do you have an understanding that prescription opioids are often prescribed to maintain a steady work flow in mines and other heavy labor occupations? Do you understand that?

A. I'm sorry. Say that question again.

Q. Sure. I want to put aside the Appalachian Kentucky point.

A. Okay.

Q. I understand what you've said about that.

We do agree with each other that West Virginia's also in Appalachia; correct?

A. Yes.

Q. And I wanted to ask you about the cause that reads in this article that you wrote, "Prescription narcotics are often prescribed to maintain a steady work flow in mines and other heavy labor occupations."

Do you see that?

A. I do.

Q. Is that a true statement?

A. I, I have not reviewed that literature in a lot of detail. I would just refer to the underlying article that is cited there for more context, which I haven't reviewed as of late. So I don't want to offer an opinion about the culture of -- the workplace culture in West Virginia.

Q. Well, I take it the intention when you wrote the article was to be accurate and to frame, frame accurately what you had determined from the literature at the time you wrote the article; correct?

A. Of course.

Q. There's also a next sentence that reads -- no, sorry. I think I asked you already about chronic pain and injury are more common in rural than in urban areas; correct? That's a true statement?

A. That was based on, on the literature that I reviewed, yes.

Q. So, so based on these considerations that are listed in this paragraph, you would expect to see higher levels of opioid prescribing in West Virginia than in many other states; correct?

A. Yes.

Q. And it's also true that these same factors could lead to different levels of prescribing within an individual state; correct?

A. I'm sorry. Can you say that again?

Q. There could be different parts of a state that might have attributes that would be more or less likely to effect prescribing levels within a state; correct?

A. Well, it would really depend on people's understandings of the risks and benefits. Just because there is opioid prescribing does not necessarily indicate that it's appropriate opioid prescribing.

And, so, there is increases in opioid prescribing when you have, for example, older populations. But that doesn't necessarily mean that that opioid prescribing was appropriate.

Q. I -- maybe I, maybe I didn't ask the right question.

A. Okay.

Q. In this paragraph that we've just been going through, you talk about different factors that might lead to higher levels of prescribing in a rural population; correct?

A. Yes.

Q. And one factor is that rural populations are on average older and, therefore, there may be more chronic pain for which management by opioid analgesics is indicated. That's one of the factors you identify in this paragraph; right?

A. Yes.

Q. And, so, within a particular state, my point is there could be parts of a state that have on average an older population than other parts of the state; correct?

A. That's right.

Q. And, so, if you had within a state variations in the population so that one part of the state had an older population, following from this factor you identified there might be higher levels of opioid prescribing anticipated; correct?

A. It's certainly possible.

Q. And the same thing could be true for a part of a state that had a heavy -- heavier manual labor component than other parts of the state. That might also lead to a higher level of opioid prescribing in one part of the state than another. Correct?

A. It's possible, yes.

Q. So within a state, there could be variations in terms of pain needs based on the nature of the population and the nature of the work?

A. No, that's not the testimony. I was not speaking of pain needs. I was talking about opioid prescribing.

Q. Within a state there could be -- I, I was asking you about pain needs. I believe your, your article here is talking about pain needs based on attributes of the population; correct?

A. There's two factors. One is pain needs and one is opioid prescribing. Those are not synonymous.

Q. Well, I'm asking about pain needs. You understand that

a relatively older population might have higher pain needs; correct?

A. Yes.

Q. And a relatively more obese population might have higher pain needs; correct?

A. It's possible.

Q. And a, and a population that has a relatively heavier manual labor component to its work might have higher pain needs; correct?

A. That's possible.

Q. And, so, within a given state, there might be differences because the population is different for different parts of the state or the work is different for different parts of the state; correct?

A. That's correct.

Q. Let me ask you to look at Page 2 of the article, please.

On the -- at the bottom of the middle paragraph there's a sentence that reads, "Increased medical use of prescription opioids has resulted in increased access to opioids for non-medical use, either through the non-medical use of legitimately acquired prescriptions or through formal or informal distribution networks."

Do you see that?

A. I do.

Q. And that's a true statement; correct?
A. That is, that is based in the literature, yes.
Q. And, so, the reference here to formal or informal distribution networks, that's a reference to family and friends or drug dealers; correct?
A. I would say -- or any kind of social network. I mean, I think we talk in this article about kind of the social networks and differences across urban and rural populations that would interact with opioid supply. So family, friends, people selling drugs, I would say all of those would be included in the informal network.
Q. And what would be included in the formal network that you're referring to here? Is that referring to drug dealers?
A. That would include drug dealers, yes.
Q. Let me ask you at the top of that next column, to the right-hand column, first sentence, --
A. I'm sorry. Can I actually qualify that previous statement? Because further on in the article, or in the paragraph I also provide -- I use pill mills and high-volume prescribers and clinics as another example of formal distribution networks.
Q. Okay. That's over on the next column; right?
A. Yes. I'm sorry. I should have noted that earlier.
Q. So that the -- you're saying that your reference to a

formal distribution network could include a drug dealer or a pill mill? Is that what you're saying?

A. That's right.

Q. There's a statement at the top of the right-hand column, "Studies indicate that the large majority of adults who use opioids non-medically obtain them from friends and relatives or from street-level dealers."

Do you see that?

A. I'm sorry. What page?

Q. It's at the very top of the right-hand column, the first sentence.

A. Of Page 2?

Q. Yes, sorry, yes. Do you see that?

A. Oh, I do.

Q. That's a true statement; correct?

A. Yes. Many people obtain opioids through friends and relatives and street-level dealers.

Q. And this is occurring after the pills have either been dispensed by a pharmacy or illegally trafficked by dealers; correct?

A. Again, I think I, I mentioned this before. The data that these are based on and that -- I think the Inciardi study is the one that I would particularly point to relies on people just reporting where they obtain their opioids. And, so, where the family and friends obtain the opioids is

not covered in the article.

Q. But these would be family and friends who have somehow obtained the opioids after they had been dispensed out of a pharmacy; correct?

A. That's what I'm saying is I don't think that that's covered in the article.

Q. And you don't have any knowledge of that one way or the other?

A. I'm relying on the literature. So I'm trying to report faithfully what the literature says. And usually they ask people where they obtain opioids. And if they say family or friends, they don't go to the family or friends and see at what point it arrived in the community.

Q. There's a statement, the next sentence, "A substantial proportion of overdose deaths and emergency department visits occurs among individuals who have never received a prescription."

Do you see that?

A. Yes.

Q. And that's a true statement; correct?

A. Yes, that's what the literature indicates.

Q. So it's an accurate reflection of what the literature was telling you?

A. Yes.

Q. You testified last week about a study done by

Christopher Ruhm showing the economic conditions are less than 10 percent responsible for the opioid crisis; correct?

A. That's right.

Q. And Christopher Ruhm did an econometrics study where he was looking at economic factors that may interrelate with prescription opioid abuse; correct?

A. I believe it was prescription opioid distribution.

Q. Are you aware that Ruhm only considered the impact of economic conditions and not any of these other factors that you've discussed in this paper that we're looking at right now?

A. I, I believe that the Ruhm article also discusses other factors, including the illicit drug supply.

Q. But you're aware that the way Ruhm measured factors, he was trying to explain what might lead to opioid use variation in different parts of the country; correct?

A. I'm sorry. Say that again.

Q. Ruhm was trying to explain factors that might lead to variations in opioid use in different parts of the country; correct?

A. If you have the article, I'd like to see it.

Q. I do.

MR. HESTER: May I approach, Your Honor?

BY MR. HESTER:

Q. Here it is.

A. So I'm looking at the key --

Q. Let me --

A. I didn't catch the question.

Q. Let me just set the table first.

Dr. Keyes, I've handed you a document marked as Defendants' West Virginia Exhibit 2344 headed on the first page, "Deaths of Despair or Drug Problems?" Christopher Ruhm.

Is this the Ruhm paper that you were referring to in your testimony last week?

A. Yes.

Q. And, and the Ruhm paper was undertaking to evaluate factors that might cause increased drug overdose deaths; correct? And I, I can point you -- it's not a trick question. It's a thick paper. But I can point you to -- if you look at Page 7 using the small numbers on the left.

A. Okay.

Q. And in the middle of the paragraph Ruhm has a reference, "Third, in the preferred specifications changes in economic conditions explain less than one-tenth of the observed increase in drug deaths."

Do you see that?

A. Yes.

Q. And that's my point is that Ruhm was trying to look at changes in economic conditions that might explain drug

deaths; is that correct?

A. That's one finding of the article. There are four. But that is one finding of the article.

Q. And he based his equations -- there's equations all through this article; correct?

A. There are.

Q. And he based his analysis on measurements of economic conditions; correct?

A. In addition to the factors that he controlled for, which were the ones that you mentioned in the previous article.

He controlled for age, morality. He had a nine-level variable controlling for population density, race, college education, gender, Hispanic ethnicity; a seven-category variable for age which would account for your -- what you mentioned earlier about the age differences across populations if one county had more older folks than another county.

Q. But --

A. He also looked at the proportion of households headed by females. Sorry. Do you want me to keep reading?

Q. No. I was just going to say -- to take a simple, concrete example, Ruhm did not measure, for instance, differences in the nature of the manual labor in different parts of the country?

A. I believe there are labor codes in the paper. I know Ruhm has done quite a few papers on labor markets. So I haven't read this article in detail --

Q. Okay.

A. -- before here, but I -- Ruhm has done pretty extensive evaluations of labor markets in rural counties and how that contributes to drug overdose.

Q. Did you know -- I'm correct, am I, that Ruhm did not have measurements of pain needs in different parts of the country in his, in his equations; correct?

A. Well, I would say that there are proxies for that based on what you mentioned before such as age and underlying medical conditions that would be indicated by these different demographic and other clinical categories that were included in the control variables.

Q. But not, for instance, nature of the work?

A. Again, I think that to the extent that labor codes were included in this analysis, that would be accounted for.

THE COURT: We're going to need to take a break when you get to a stopping place.

MR. HESTER: All right, Your Honor. This is a good place for me.

THE COURT: Is this a good place?

MR. HESTER: Yes. Thank you.

THE COURT: Okay. Let's be in recess for about 10

minutes.

(Recess taken at 10:24 a.m.)

THE COURT: All right, Mr. Hester.

MR. HESTER: Thank you, Your Honor.

BY MR. HESTER:

Q. Dr. Keyes, I wanted to be clear on one point, that you have not identified any sources of diversion in relation to shipments between distributors and pharmacies; is that correct?

A. I have not covered that in my report.

Q. And you've not identified any such diversion between the time that a distributor has the pills and the time it delivers to a pharmacy, correct?

A. I'm aware that that occurs. I mean, there are thefts that occur on -- that that happens, so that would be a source of diversion.

Q. But you've not identified any such sources, correct?

A. Other than that it occurs and it's included in my definition of diversion.

Q. Could we pull up the deposition from this litigation, please, Page 113? Page 113, Line 13. Dr. Keyes, I started off the question and said, "Right, but I wanted -- just to be clear", and I think so we're talking the same language here and then I asked you this question. "I want to be clear that you're not identifying any sources of diversion

in relation to shipments between distributors and pharmacies. You haven't identified any such evidence?" And your answer was, "Right." Was that correct when you -- was that a correct answer when you gave it?

A. I don't think so. I mean, I know in the Inciardi article, in the introduction, it does specifically talk about theft. You know, so I think if I were answering the question today, which I am, I would point to -- there have a couple sources in the Inciardi 2008 introduction about -- about that type of diversion. So, I think that I would -- I would qualify that answer today.

Q. My question is, when you gave that answer, were you under oath?

A. Yes.

Q. And when you gave that answer, did you mean to be answering correctly and truthfully?

A. I meant to be answering correctly and truthfully.

Q. And that's the answer you gave when I asked you, "You're not identifying any sources of diversion in relation to shipments between distributors and pharmacies? You haven't identified any such evidence?" And your answer was, "Right." Is that correct?

A. That was my answer.

Q. And that was meant to be truthful when you gave it, correct?

A. I hadn't remembered the Inciardi article and the references that were in that introduction.

Q. Dr. Keyes, was that meant to be truthful when you gave the answer?

A. It was meant to be truthful.

Q. Let me ask you, Dr. Keyes, a couple of preliminary points around doctor prescribing activity. Doctors decide on the dosage strength to include in a given prescription, correct?

A. Can you say the question again?

Q. Sure. Doctors decide on the dosage strength to include in a particular prescription, correct?

A. Yes.

Q. And also, doctors decide how many pills to include in a given prescription for opioids, correct?

A. That's right.

Q. In other words, a doctor makes the judgment whether to include a 10-day supply, a 30-day supply, or some other duration for the prescription of the opioid, correct?

A. A doctor makes the decision about that, yes.

Q. And your view is that the overwhelming majority of doctors prescribe opioids to their patients in good faith, correct?

A. I don't know what proportion prescribe in good faith but I would -- my opinion would be that it would be a

majority who make prescriptions based on the information that they have.

Q. Well, let me ask it again just to be clear. Your view is that the overwhelming majority of doctors prescribe opioids to their patients in good faith, correct?

A. Yes. I -- I think that that is true. They base it on the decision -- the information that they have.

Q. And starting in the late 1990s up through around 2010, doctors increased their prescribing of opioids, correct?

A. Yes.

Q. And you wrote in your report at Page 23, if you want to look at it, but I'll quote it to you. I think it will sound familiar to you. "Pervasive over-prescribing resulted in unused prescription opioid medicines diverted for monetary value, bartered or for no cost among family and individuals in a shared social network." Do you want me to point you to that passage?

A. Yes, if you don't mind. I'm on Page 23.

Q. Yes. So, it's at Page 23 of your report. Let me see if I can find it. It's in the middle of the page, Dr. Keyes. There's a -- there's a bolded sentence.

A. I -- yes. It's at the top of my Page 23. Maybe we have different versions.

Q. Oh, yes. Yes. You're right. Absolutely. At the top, the sentence that -- and there's a sentence that's bolded

and it says, "Pervasive over-prescribing resulted in unused prescribed opioid medications diverted for monetary value, bartered, or for no cost among family and individuals in a shared social network." Do you see that?

A. I do.

Q. And that's a true statement, correct?

A. That's my read of the literature.

Q. And the reference there to diverted for money, barter, or no cost, that's diversion after the pills have either been prescribed or illegally trafficked into the community, correct?

A. With regard to over-prescribing, that is specifically focused on prescribing behavior. There's another section, oversupply.

Q. So, your point is that there was a pervasive over-prescribing that led to unused pills and then they went from the people who were prescribed those pills to others, either through barter, through money, or through giving them away, correct?

A. That's one source of the oversupply.

Q. And you also state in just a few sentences down in this same paragraph of your report that, "Available estimates indicate that 90 percent of patients prescribed opioids after surgery have unused medication, most of which is not disposed of or stored safely." Do you see that?

A. I do.
Q. And that's a true statement, correct?
A. Yes.
Q. And that's based on your --
A. In the literature that I read.
Q. Yeah. And so, when you -- when you say in the literature you've read, you're purporting to give an accurate summary of the literature when you state this?
A. I'm purporting to, yes.
Q. And that's your best effort?
A. Yes. I always update, you know, my opinions and information with new -- new information as I'm gathering it. So, I just want to be clear that I'm basing my statement on the literature as I've read it.
Q. But when you wrote your report you meant to be accurately reflecting the literature as you know it at the time?
A. I certainly did.
Q. And the point you're making here in this sentence about available estimates indicate that 90 percent of patients are prescribed opioids have unused medication after surgery, the point you're making there is that even though there might be an underlying legitimate need for the prescription opioid, the doctor prescribes too many pills to meet the need, correct?

A. It's not referring to the legitimacy of the need. It is referring to the -- the -- that there were too many pills prescribed but I'm not -- that these studies did not ascertain the legitimacy of the prescription itself, only that there were unused medications. So, it could also be that the prescription wasn't needed and that there were unused medications.

Q. You're aware that many times prescription opioids are prescribed for people after surgery to deal with acute pain, correct?

A. It depends on the type of surgery. The amount of prescription opioids that are prescribed depends on what surgery we're talking about. There's many different kinds of surgery.

Q. My question was narrower and probably simpler than that, which is you are aware that prescription opioids are often prescribed for treatment of acute pain after surgery, correct?

A. Again, I think that that's too broad of a statement.

Q. You're not aware of that?

A. I am aware that opioids can be prescribed after some surgeries.

Q. And so, the point is, there may be a surgery where prescription opioids are prescribed to deal with the pain after surgery, but in your review of the literature, you

determine that in 90 percent of those cases there were unused medicines left after the person used them for treating pain?

A. That's right.

Q. And that's a judgment being made by the doctor about how many pills to include in that prescription for the surgery, treatment of the pain following surgery, correct?

A. That's right.

Q. And so, this could happen quite often, correct, that there might a circumstance where a prescription is written and a doctor writes too many pills for that given prescription, correct?

A. Yes.

Q. And the physician, in the good faith exercise of judgment, decides to prescribe an opioid to meet a particular need for a particular kind of pain, correct?

A. Can you state the question again?

Q. Yes. So, you could have a circumstance, I take it there's many circumstances where a doctor could make a legitimate good faith decision to prescribe opioids to deal with a particular kind of pain, correct?

A. As I've said before, the doctor is making a determination based on their understanding of the risks and benefits of a particular opioid prescribing, which itself has changed over time. You know, certainly, the

recommendations for prescribing have changed quite a lot over the last ten years. And so, I'm not arguing that there are not doctors that are acting in, quote-unquote, "good faith" to write, quote-unquote "legitimate prescriptions", but that that -- these studies are not purporting to report on the efficacy or legitimacy of a particular prescription. That's a separate evidence base.

Q. But going back to what we established a few minutes ago, your view is that the overwhelming majority of doctors prescribe opioids in good faith, correct?

A. Yes. I think many doctors are doing their best.

Q. The overwhelming majority, correct?

A. Certainly, yes, the majority.

Q. The overwhelming majority, correct?

A. Yes.

Q. And then the doctor acting in good faith to prescribe the opioid may provide for more pills in that prescription than are needed to meet the need for which the pills are being prescribed, correct?

A. That can happen, yes.

Q. And in that case, even though the doctor has decided that the medical need is legitimate, the doctor has prescribed more pills than are needed to meet the need, correct?

A. The doctor has made a determination of a medical need

and has prescribed too many pills in that circumstance that you're -- this hypothetical that you're offering.

Q. And so, at Page 23 of your report, again, the same page, the same paragraph, actually, you state that, among non-medical opioid users interviewed about where they obtain their opioids, 50.5 percent report from a friend or relative.

Do you see that? It's almost exactly in the middle of that paragraph. It's the sentence that begins data from the National Survey on Drug Use and Health.

A. Yes. 50.5 percent receive -- in that survey received prescription opioids from a friend or family.

Q. So, let's just be clear on what that is. It's a survey from the National -- from the organization called NSDUH, which is the National Survey on Drug Use and Health, correct?

A. That's the -- the name of the survey is NSDUH.

Q. And that's a government survey that's run --

A. Yes.

Q. -- periodically?

A. Annually.

Q. And in that survey the report is that 50.5 percent of non-medical users of opioids stated that they obtained the opioids from a friend or a relative, correct?

A. Among the respondents in that survey, yes.

Q. And your analysis in the report of this passage was that quite a bit of that was the result of unused medications after a particular prescription, correct?

A. My analysis included unused prescriptions. The previous sentence uses that statistic in citing evidence for the proposition that the expansion of opioid sales and distribution served as a catalyst for the overall availability and one consequence would be unused medication.

Q. So, you would have unused medication that would be a ready source of diversion to others from family and friends, correct?

A. That's one pathway, yes.

Q. You also state just a -- I think in the next sentence that the NSDUH data showed -- oh, sorry. Let me go down two sentences further. There's another sentence that reads, "Data from the NSDUH show that 57 percent of non-medical opioid users in 2007 obtained opioid -- opioids from family or relative for free with another 9 percent reporting that a friend or a relative for purchase was also a source of the opioids."

Do you see that?

A. I do.

Q. So, and that's a true statement, correct?

A. That is. Well, sorry. It's like -- it's based on my review of the literature or I guess my reading of those

statistics from the NSDUH.

Q. Right. So, you're accurately reporting what NSDUH reported, correct?

A. Yes.

Q. And the point is, so that would add up to 66 percent of non-medical users obtaining pills from friends or family in 2007, correct?

A. Not exactly. That -- the survey -- it was not a mutually exclusive category. People could report all of the sources they obtained opioids from, including a doctor, friends and family, a drug dealer; and then friends and family for free, friends and family for money.

So, it's not -- can't add them up. You know, there's going to be overlap. Some people got them for free from family or friends and then, later on, they bought them from a friend. You know, so --

Q. I see. I see what you're saying. So, but the point is, the survey reflected, again, that more than half of the people who were non-medical users, in other words, people who are using opioids without a prescription, more than half reported they had obtained the opioids from a friend or relative for free, correct?

A. That's true, but that's not the -- that might not be the only source. But that is a source. It's a -- it's a very common source for opioids.

Q. So, fair enough. So, somebody who is a non-medical opioid user might get some for free from family, but then might also go out on the street and buy some more, correct?

A. Well, I think more germane to the discussion, most non-medical users also obtain opioids medically. So, there's a large overlap between those two. They're not distinct. You don't have one group of legitimate opioid users and one group of non-medical users. There is a lot of overlap between those two groups.

Q. But you would have -- you could have a circumstance where somebody is a non-medical user, they might have a prescription for some, but then they obtain other pills from family or friends for free, correct?

A. That's right.

Q. Or you could have a circumstance where somebody has a prescription for opioids, but they also go out and buy opioids on the street, correct?

A. That is a -- that is a scenario that occurs.

Q. And they're non-medical users, so they -- by definition, they are using opioids for some non-medical purpose, correct?

A. That's right.

Q. And your view is that the high volume of opioid prescriptions that doctors were writing became the foundation for the overall expansion of the opioid supply,

correct?

A. Can you say that sentence again?

Q. Yes. Your view is that the high volume of opioid prescriptions that doctors were writing became the foundation for the overall expansion of the opioid supply, correct?

A. That is a major source of the foundation, yes.

Q. And, in your view, it is -- it was a principal foundation of the expansion of the supply of opioids, correct, the prescribing by doctors?

A. I think it's a major foundation of the increases in prescribing and, you know, what we saw subsequently with the heroin epidemic.

Q. And your view is that the high volume of opioid prescriptions also became the foundation for the overall expansion and opioid-related harm, correct?

A. The high volume of prescribing was a foundational source of the epidemic that followed, including our current fentanyl epidemic.

Q. And it was the foundation for the overall expansion and opioid-related harm, correct?

A. Yes. It was a principal source. I would say there's other sources. You know, it's a -- in these epidemics where you have a lot of different underlying and interacting factors, certainly, the pervasive over-prescribing was one

of the foundational ones.

Q. And one of the foundational ones in particular for the expansion of opioid-related harm was the level of prescribing by doctors, correct?

A. The level of prescribing by doctors certainly contributed to the availability of opioids in the community. So, I would say that that is a true statement, but it is not exclusive of other sources of prescription opioids, as I've outlined and we've discussed.

Q. But let me -- let me be clear on it. Just let me ask it one more time. You agree that the high volume of opioid prescriptions became the foundation for the overall expansion in the opioid supply and opioid-related harm, correct?

A. Yes. I believe I've written that before, but in context, I would just say it's a foundation.

Q. Yes. So, your answer is yes to my question?

A. Yes.

Q. And then, your view is that the opioid crisis would not have occurred if prescribing opioids had not become standard practice in managing acute and chronic pain, correct?

A. That's right.

Q. Distributors did not ship more pills than doctors prescribed, correct?

A. I haven't evaluated the distributor shipments, so I

wouldn't want to comment on them. I don't have an opinion on that.

Q. You're aware, I take it, that no matter how many opioids a distributor ships to a given pharmacy, if there's not a prescription from a doctor, those opioids stay on the pharmacy shelf and never reach the community, correct?

A. My understanding generally is that that's how it's supposed to work. I don't know exactly how it worked in every circumstance here.

Q. Well, let me ask it again just to make clear. No matter how many opioids a distributor ships to a given pharmacy, if there's not a prescription from a doctor, those opioids are supposed to stay in the pharmacy and not go out to the public, correct?

A. They certainly are supposed to.

Q. And so, you -- the answer is yes?

A. Yes.

Q. You published an article in 2013 that said, "The data are robust in demonstrating that rates of overdoses are proportional to the rates of prescribing", correct?

A. Which article is this?

Q. I'm not sure if I have that article right handy. Do you remember publishing such an article that said that, "The data are robust in demonstrating that rates of overdoses are proportional to the rates of prescribing"?

A. I certainly agree with the statement. I would just prefer to see the article if I'm going to be quoted to make sure I'm --

Q. Okay. So, you agree with this statement that rates of overdoses are proportional to the rates of prescribing of opioids?

A. Yes.

Q. Dr. Keyes, I think we've talked about this before, but you do understand that drug trafficking organizations and drug dealers illegally supply prescription opioids in Huntington and Cabell County, correct?

A. You said illegally?

Q. Yes.

A. Yes.

Q. And those illegal acts expand the total supply of prescription opioids in Cabell County and Huntington, correct?

A. Say -- say the question again.

Q. Yes. Those illegal acts of drug trafficking into Cabell County and Huntington expand the total supply of prescription opioids in the community, correct?

A. Yeah. There's literature on this in my report. I mean, certainly, it's a minority. The analyses that have been done suggest that it's a minority of all of the opioid-related harm in the Cabell-Huntington community.

But, certainly, there is illegal trafficking that occurs and that does contribute to harm.

Q. And the illegal trafficking also expands to the total supply of prescription opioids, correct?

A. To -- yes. There's a -- I would say it's minority of the total supply, certainly, but it certainly does contribute to it.

Q. Contribute to the supply of opioids, correct?

A. It contributes to the supply of opioids, yes.

Q. And so, drug trafficking also contributed to the opioid-related harms that you identify, correct?

A. Yes.

Q. And we talked before about the fact that drug dealers make and sell counterfeit opioid pills, correct?

A. They can.

Q. And that includes counterfeit opioid pills that are adulterated with fentanyl, correct?

A. That -- that has occurred, yes.

Q. And people have overdosed and died from those counterfeit opioid pills, correct?

A. The multiple cause of death filed in the CDC doesn't differentiate illicit from licit prescription opioids. So, I'm certainly -- it's certainly likely that someone has overdosed from a prescription opioid, but the data that I rely on in the report does not distinguish those two.

Q. Well, let me ask it again to be clear. You're aware that people have overdosed and died from counterfeit opioid pills, correct?

A. I'm sure it has occurred, but I have not reviewed data on specific counterfeit opioid overdoses.

MR. HESTER: Could we cull up the deposition, please, from this case, Page 324?

BY MR. HESTER:

Q. Dr. Keyes, let me point you to Line 3. My question was, "And are you aware that people have overdosed and died from pills like that?" And if you need me to go back and show you the context, I can, but this is discussing counterfeit pills. That was my question.

Do you see that?

A. Yes.

Q. And your answer was, "Yes, I have. I'm aware that that occurs."

Do you see that?

A. I do.

Q. And was your answer correct when you gave it?

A. Yes. That's -- I think it's consistent with what I've just reported.

Q. And so, these counterfeit pills also expanded the supply of opioids in Huntington and Cabell County, correct?

A. Yes. I think it's a minority contribution to the

supply, a small minority.
Q. But you don't know the percentage of prescription opioids in Huntington and Cabell County that -- that were counterfeit, do you?
A. Well, we can estimate it somewhat from the data, which I have tried to do in the report and which I believe is reflected in that testimony, as well, that based on what we know about what people report in terms of where they obtain opioids, I would say it's maybe 10 percent, I think somewhere around there.
Q. Would be counterfeit opioids?
A. Well, would be illicit opioids.
Q. Which would include counterfeits?
A. Which would include counterfeit.
Q. But that could also include counterfeits that are laced with fentanyl and might be more lethal than a conventional prescription opioid, correct?
A. Well, the lethality of the opioid is really determined by the dose. So, the probability of an overdose is dependent on the dose of the opioids that you take. And so, a conventional opioid and an opioid laced with fentanyl, for example, if they had a different dose, then that would change the overdose risk.
Q. Do you have any understanding whether a counterfeit pill laced with fentanyl is more or less risky than a

conventional prescription opioid pill?

A. Well, I think that's comparing apples and oranges. So, if we're comparing two doses, you know, a conventional prescription opioid pill compared to a counterfeit pill that has opioid -- has fentanyl in it, if the fentanyl pill has a larger dose, which it probably does if it has fentanyl, then it would be riskier. But I don't think you could compare the pills directly unless you're comparing -- unless they have equivalent doses.

Q. Let me flip to a slightly different topic and it builds on something you said a few minutes ago. You're aware that there are different dosages for opioid medications, correct?

A. Yes.

Q. And so, there may be different judgments made by a doctor in prescribing opioids about what dose to use for a particular patient, correct?

A. Yes. A doctor would make -- two doctors might make a different decision about the dosage.

Q. And the doctors are the ones who make the judgment about what dose should be prescribed for a particular patient and a particular need, correct?

A. Yes, based on the information that's been given to them.

Q. And opioid medications can also be prescribed for different durations, correct?

A. That's right.

Q. For instance, a prescription to treat acute pain with opioids might be for a different duration than a prescription to treat some longer-term pain, correct?

A. I wouldn't make a blanket statement because there's been plenty of acute conditions that people have gotten quite a long duration of opioid pills for. So, it would really depend on the condition, the doctor, and what condition we're comparing it to.

Q. But the doctor will make the judgment both about the dose and the duration for a particular prescription or for a particular regimen of treatment, correct?

A. A doctor would make the decision based on the information available to him or her.

Q. And you are aware that opioids are used to treat different kinds of pain beyond chronic pain, correct?

A. Am I -- say that -- that question again, please.

Q. You are aware that opioids are used to treat different kinds of pain beyond chronic pain?

A. I'm aware that they are used.

Q. To treat different kinds of pain beyond chronic pain?

A. Yes.

Q. And not every patient treated with opioids uses them chronically or for a long time, correct?

A. That's right.

Q. And so, some patients might use prescription opioids only for a few days or for quite a short period of time, correct?

A. It's certainly possible that there's -- well, the literature shows that there are people who use for a short duration and people who use for a long duration. So, yes, there are people who use opioids for a short duration.

Q. You testified on Friday about an article by Edlund and colleagues that provides information on the incidence of OUD based on different levels of dose and duration, right?

A. Yes.

Q. And when you talk about incidence of OUD, that means new OUD; in other words, how many people develop OUD after they receive an opioid prescription. That's -- that's what you mean by incidence, right?

A. OUD is typically episodic. And so, I believe in the Edlund article they were looking at new episodes of Opioid Use Disorder.

Q. So, in other words, it would be Opioid Use Disorder that arises in some percentage of people after they're exposed to prescription opioids?

A. That's right.

Q. So, let's take a look at that Edlund study, please.

MR. HESTER: May I approach, Your Honor?

BY MR. HESTER:

Q. Dr. Keyes, we've handed you what's been marked as DEF-WV-2307. On the first page it's headed The Role of Opioid Prescription in Incident Opioid Abuse and Dependence Among Individuals With Chronic Non-Cancer Pain.

Do you see that?

A. And the second part is The Role of Opioid Prescription.

Q. Right. And this is the Edlund article that you were referring to in your testimony last week, correct?

A. Correct.

Q. And you consider this article to be accurate, correct?

A. Based on my reading of it, I have judged it to be of -- scientifically meritorious, I would say.

Q. And you testified last week that it's relied on by epidemiologists in your field when performing research on opioid use and Opioid Use Disorder, correct?

A. Yes.

Q. And you also testified that this article is respected and not subject to any underlying questions of veracity, correct?

A. Not that I'm aware of.

MR. HESTER: Your Honor, I would move this document into evidence.

THE COURT: Any objection?

MR. FARRELL: Judge, I'm not quite sure it's proper to admit medical literature into the record as

evidence. I'm not necessarily opposed to it, but you'll recall that the defendants objected to me even showing you the medical literature, let alone entering it into the record. So, I'm a little befuddled as to the purpose of and the propriety of entering medical literature into the record at this stage.

MR. HESTER: Well, Your Honor, the witness testified last week that this is a respected article, that there are no issues of underlying veracity or accuracy to her understanding with this article, that it's relied on by epidemiologists in the field. It was highlighted in the testimony presented on Friday to the Court.

It seems to us that, given the witness's testimony, it satisfies the residual hearsay exception because we've -- the record now demonstrates sufficient indicia of trustworthiness as to this document.

We also think it would be helpful to the Court because it has been highlighted and discussed at some length and it feels, to us, helpful in the sense of the Court being able to rely on the document and to -- and to have it available in the record.

THE COURT: Mr. Farrell?

MR. FARRELL: Well, Judge, you're the trier of fact. And so, I think that the purpose of the hearsay rules is in general to keep out of the record items that are not

reliable or trustworthy and I am fully confident that Your Honor has the ability to apply appropriate weight but, again, this is not a non-traditional procedural aspect of the case.

Of course, I'm accustomed to jury trials and not bench trials. So, I'll leave it to Your Honor's discretion whether you think it will assist you and, if it does, I have a host of other medical journals that I would like to supplement when it's my turn to re-direct.

MR. HESTER: Well, Your Honor, I'm not -- I'm not purporting to offer some sort of deal to Mr. Farrell. It just seemed to me that the witness gave quite a bit of specific testimony on this specific document that makes it different from the norm of any piece out of the literature because she specifically spoke to the reliability and veracity of this particular document.

THE COURT: Well, I don't think you've got this within Rule 807, Mr. Hester, so if there's an objection to it, Mr. Farrell, I'll sustain the objection.

Is there an objection to it?

MR. FARRELL: Yes. Yes.

THE COURT: Well, I'm not going to admit it but, Mr. Hester, it's fair game for you to question her about it.

MR. HESTER: Thank you, Your Honor. I'll do it that way. That's totally fine.

THE COURT: Okay.

BY MR. HESTER:

Q. Dr. Keyes, I know you're familiar with this, but I think we need to put in some pieces into the record just to clarify the nature of this study. So, the study focused on adults 18 and over with a new chronic non-cancer pain episode and no opioid use or OUD in the prior six months; is that correct?

A. That's right.

Q. And the sample included 568,640 individuals in total, correct?

A. Yes.

Q. And that's a relatively large sample size for a study like this, correct?

A. For a study like this that is based on medical records, I would say it's fairly standard, but it is, you know, a large sample size.

Q. And the study was -- I can point you to Page 4, but you may know this one out of your head. This study was designed to measure the incidence of OUD following exposure to different levels of prescribed opioids, correct?

A. Yes.

Q. And it reports levels of incidence OUD; in other words, new OUD for both acute and chronic pain treatment, correct?

A. Yes.

Q. And here, when the article refers to acute, it refers to the length of the opioid therapy, correct?

A. That's right.

Q. So, it's not -- when it uses the term "acute", it's not referring to the type of pain, but the duration of the treatment, correct?

A. Yes.

Q. And it defined acute as treatment for less than 90 days with prescription opioids, correct?

A. It was inclusive of 90 days. So, 90 days or less.

Q. Got it. We're with you. We're with each other. So, 90 days or less would be defined in this study as acute treatment, correct?

A. That's right.

Q. And so, chronic treatment was -- 90 days or more was considered chronic in this study, correct?

A. More than 90.

Q. So, more than --

A. So, 91 or more.

Q. Thank you. Thank you. So -- so, let's look at the results and we can see the results at Page 3 of the document discussing the results and the first full paragraph in the right-hand column. Let me confirm, Dr. Keyes, that for acute or short-term pain treatment; in other words, 90 days or less, the rates of new OUD were .12 percent for patients

who were treated with a low dose, correct?

A. I'm sorry. Which page are you on? I just want to make sure that I --

Q. I was looking at Page 3.

A. I'm sorry. I was looking at Page 4.

Q. In the right-hand column and the third sentence. This refers to the unadjusted rates of post-index OUD diagnosis. Do you see that?

A. Yes.

Q. And so, when we talk about post-index OUD diagnosis that's referring to the -- to the percentage of people who were treated with a given dose duration of prescription opioids and it's referring to the percentage of people who developed OUD, correct?

A. That's right.

Q. And so, the results reflect that there was a -- an incidence of .12 percent for patients who were treated with a low dose for less than 90 days, correct?

A. That's right.

Q. And .12 percent, as well, for patients treated with a medium dose for 90 days or less, correct?

A. .12, yes.

Q. And the same is true for patients treated with a high dose for 90 days or less, that the incidence level of OUD was .12 percent, right?

A. That's right.

Q. And so, turning that around, that -- that means that over 99.8 percent of patients who were treated with prescription opioids, no matter what the dose, did not develop OUD if they were treated for less than 90 days, correct?

A. That's right.

Q. Now, let's look at the other side of the coin, chronic or longer term treatment. So, more than 90 days. And the rates of OUD there were .7 percent for patients who were treated with a low dose for more than 90 days, correct?

A. That's right.

Q. And the rate of OUD was 1.2 percent for patients who were treated with medium dose for more than 90 days, correct?

A. Yes.

Q. And the OUD level was higher for patients with a high dose treated more than 90 days, 6.08 percent, correct?

A. I see 6.1 percent, but maybe that's rounding.

Q. It may well be rounding, but okay. I pulled that out of one of the tables.

A. Okay.

Q. But 6.1 percent is stated here. So, just so we're on the same page, so it found a level of OUD incidence for people treated more than 90 days as a high dose and that

came out to 6.1 percent, correct?
A. That's right.
Q. And when you talked last week about the 122 times, you were using this number of the 6.08 percent, correct?
A. That's right.
Q. You weren't referring to these other numbers, the numbers, for instance, for acute -- acute treatment of less than 90 days of .12 percent? That's not what you were referring to, correct?
A. The 122 times is comparing the high dose chronic group to non-prescribed opioid group, but the other groups also had an increase in the risk, including the group that you mentioned first, the acute low dose group. They were more than three times as likely to develop Opioid Use Disorder.
Q. So, but focusing on the percentages here, the study did find a percentage of .12 percent of OUD when opioids were used for less than 90 days at all dosage levels?
A. Right, which the authors mention in the discussion translates to, you know, 98 million people are prescribed opioids in the United States. So, that translates to a major population impact.
THE COURT: Your Honor, I move to strike as non-responsive.
THE COURT: Just a minute. Overruled. Go ahead.
BY MR. HESTER:

Q. So, but -- but let me -- let me just be clear, Dr. Keyes, on what the findings were. So, the study found that the incidence level of OUD when opioids were used for less than 90 days at any dosage level was .12 percent, correct?

A. That's right.

Q. And the study also found that when opioids were used for more than 90 days with a low or medium dose the incidence of OUD was between .7 percent and 1.2 percent, correct?

A. That's right.

Q. So, then meaning when opioids were used for more than 90 days at a low or medium dosage, 98.8 percent of the patients did not develop OUD, correct?

A. That's right.

Q. And these findings from this study apply to West Virginia, correct?

A. I think that -- I generally think that they would generalize beyond the study sample.

Q. And so, you agree that the findings of this study, this Edlund study that we're looking at, apply to West Virginia, correct?

A. Yes.

Q. And the -- let me point you to Page 6 of the document, please. At the top of the page, the Edlund -- Edlund and the other authors state, "Actual frequencies of OUDs were

relatively low; that is, under 1 percent for four of the six categories of opioid use."

Do you see that?

A. Well, that's not the whole sentence. The sentence starts, "Although risks were high." It could be argued that actual frequencies of OUDs were low.

Q. Well, okay. If you're going to -- if you're going to add to my question, you need to put in the parenthetical, too.

A. I'm sorry. I'll read the whole thing. "Although risks as measured by ORs", which means odds ratios, "it could be argued that actual frequencies of OUDs were relatively low; that is, under 1 percent for four of the six categories of opioid use."

Q. Yes. So -- so, we both are -- we see that sentence and now I wanted to ask you a follow-up on the sentence, which is it accurate to state that the frequency of OUD was under 1 percent for four of the six categories of opioid use, correct?

A. That's right.

Q. And so, when we talk about the categories of opioid use, there's six categories we're talking about? There's three that could be more than 90 days and three that would be 90 days or less, correct?

A. That's right.

Q. And the three in each bucket would be low, medium, high, less than 90 days, low medium high 90, days or more, or 91 days or more, correct?

A. That's right.

Q. So, that's what they mean by the four of the six categories, correct?

A. Yes.

Q. Then it goes on in the next paragraph. There's a first sentence that says, "Our findings have important clinical implications, as they suggest that the risk of an incident OUD is relatively small for an acute trial of opioids."

Do you see that?

A. I do.

Q. And, again, there they're referring to an acute trial, meaning that any dosing level for less than 90 days, the Edlund article characterized the risk of an incident OUD as relatively small, correct?

A. That's what that sentence says. I believe it's more contextualized in the -- in the following sentences.

Q. But the -- but Edlund did state in this article that the risk of an incident OUD is relatively small for an acute trial of opioids?

A. That sentence says that.

Q. And acute trial, again, meaning less than 90 days of use?

A. That's right.

Q. Let me also ask you to look a few sentences further down. It says, "Our data suggests that it is almost meaningless to talk of a single rate of OUDs."

Do you see that?

A. That -- that's how the sentence begins, yes.

Q. Right. I just wanted to ask you about that clause. And the point being made there is you can't talk about a single rate of OUD associated with prescription opioids because you need to know both the duration of treatment and also the level of dosing, correct?

A. My interpretation of that sentence would be that OUD risk does vary with dose and duration. I mean, certainly, there are many public health studies that have assessed overall OUD prevalence. And so, my interpretation of that would be that the author is reporting that OUD risk varies by dose and duration. So, there's not one particular number of like this is how many OUD cases you're going to get. But, certainly, in public health we report the prevalence of OUD without always reporting dose and duration because it really depends on the public health activity that you're doing.

Q. But the point being made in this Edlund study is if you're really going to be able to assess risks of OUD associated with treatment with prescription opioids, you

need to know the dose and duration?

A. No. I don't think that that's how my interpretation of that sentence would be. My interpretation would be that Edlund and colleagues are saying that dose and duration are major factors in determining the risk of OUD.

Q. Let me ask you, you're aware that the majority of opioid prescriptions are for short-term therapy of less than 90 days, correct?

A. In what year?

Q. Let me ask you generally without reference to any particular year. You're aware that the majority of opioid prescriptions are for short-term therapy of less than 90 days?

A. It certainly would depend on the opioid therapy that we're specifying. I haven't seen data on every opioid therapy.

Q. So, you don't know one way or the other what level of prescriptions are for short-term treatment as compared to longer term?

A. Because you haven't specified the product that we're talking about, I can't report on the average duration of every opioid product.

Q. Do you have any understanding that there's a large fraction of opioid prescriptions that are written for short-term treatment of less than 90 days?

A. Yes, which is why this OUD number is so concerning.

Q. The -- I was asking about less than 90 days.

A. Right.

Q. And the point is that you're aware that there is a substantial fraction of prescriptions that are written for less than 90 days of treatment, correct?

A. Yes, which is -- yes. That's the problem with having .12 percent incidence.

Q. The -- the -- and this is true even for patients with chronic non-cancer pain? They're often prescribed opioids for shorter durations, correct?

A. I don't know that.

Q. Let me ask you to look back at Edlund again. Again, sticking on Page 6. He begins on the left-hand column, the final paragraph. The first sentence says, "Although our study was designed to study incidence of OUDs, it also provides descriptive data on incident opioid use for chronic pain." Do you see that?

A. Yes.

Q. And then it goes on in the next sentence to say, "At 35 percent, incident opioid use was not uncommon" -- I'm sorry. I messed that up. "At 35 percent", comma, "incident opioid use was not uncommon among individuals with new onset of a CNCP episode."

Do you see that?

A. I do.

Q. And the reference to CNCP is chronic non-cancer pain, correct?

A. Yes.

Q. And this study is focusing on the treatment of people with chronic non-cancer pain, correct?

A. Right.

Q. And so, it indicates here that only 35 percent of the population, 35 percent of the sample they studied, only 35 percent received an opioid prescription, correct?

A. 35 percent of people on the sample were prescribed an opioid for chronic non-cancer pain; that's the question, right?

Q. Yes, exactly.

A. Okay.

Q. That's -- that's what I meant to be asking you. In other words, he was looking at a sample of people with chronic non-cancer pain and he's reporting that only 35 percent of the sample received an opioid prescription, correct?

A. I certainly wouldn't use the word only. That's a huge number.

Q. I'm -- okay.

A. The word only isn't in the sentence. That's --

Q. I'll take out only.

A. Thank you.

Q. He -- he's looking at a sample of people with chronic non-cancer pain and 35 percent of the sample received an opioid prescription, correct?

A. Yes.

Q. And so, another way to put that is 65 percent of this group that had chronic non-cancer pain was not prescribed an opioid?

A. That's right.

Q. And then, he states in the next sentence, "However, among the 35 percent who received opioids, only 5 percent proceeded to chronic use."

Do you see that?

A. I do.

Q. And then he says, "And only 3 percent of these proceeded to chronic use of high daily doses."

Do you see that?

A. I do.

Q. So, he does a little math for us in his parentheticals. He says, "Among the 35 percent who received opioids, the 5 percent who proceeded to chronic use represented 1.7 percent of the sample", correct?

A. That's right.

Q. So, he's saying there that only 1.7 percent of the overall sample was prescribed opioids for more than 90 days,

correct?

A. Again, the only is not the word I would use.

Q. He's got only in the sentence.

A. Not for the 1.7 percent.

Q. He's got only before 5 -- okay, we won't play. I'll take out the word only. I won't inject any value judgment. I'm just trying to clarify the word.

He's saying that 1.7 percent of the sample received an opioid prescription for more than 90 days, correct?

A. That's right.

Q. And he's saying within that group the 1.7 percent that received a prescription for more than 90 days for opioids, 3 percent of those people representing 0.1 percent of the overall sample proceeded to chronic use at a high dose, correct?

A. That's right.

Q. And he -- he then goes on in the next sentence to say, "This is a steep selection process for patients achieving chronic high dose therapy."

Do you see that?

A. Yes.

Q. And then he says, "Further, this selection process may be even steeper now than when our study was conducted, due to growing physician concerns regarding addiction."

Do you see that?

A. I do.

Q. And do you consider that to be a true statement?

A. I do believe that physicians are more concerned about addiction now than they were in the 1990s and 2000s.

Q. And more so than they were at the time this article was written in 2014?

A. Well, I think at the time the article was written in 2014 -- I mean, I'm agreeing with the author's statement that there is a growing concern about addiction in 2014.

Q. And that's a growing concern within the medical community as it gathered more data and information?

A. I think the medical and general public was increasingly concerned about addiction.

Q. Let me ask you to look at another article, please.

MR. HESTER: Your Honor, may I approach?

THE COURT: Yes, you may.

BY MR. HESTER:

Q. Dr. Keyes, we've handed you a document marked DEF-WV Exhibit 2524 headed Opioid Abuse and Chronic Pain Misconceptions and Mitigation Strategies. Dr. Keyes, do you have that document in front of you?

A. I do.

Q. And this is a 2016 paper written by Nora Volkow and others published in the New England Journal of Medicine; is that correct?

A. Yes.

Q. And you rely on this article in forming your opinions in this case, correct?

A. I do.

Q. And Nora Volkow is the Director of the National Institute on Drug Abuse, correct?

A. Yes.

Q. And let me point you to Page 1 of the document under the heading for Source of the Opioid Epidemic. There's a third sentence that reads, "In 2014 alone, U. S. retail pharmacies dispensed 245 million prescriptions for opioid pain relievers."

Do you see that?

A. Yes.

Q. Does that accord with your understanding?

A. It does.

Q. And then, it goes on to say, "Of these prescriptions, 65 percent were for short-term therapy of less than three weeks."

Do you see that?

A. Yes. That's exactly why the Edlund article should be so concerning.

MR. HESTER: Your Honor, I move to strike as non-responsive.

THE WITNESS: I can explain.

THE COURT: Well, answer --

Mr. Farrell?

MR. FARRELL: Yeah. I think she should be permitted to explain. She gave the -- she answered the question yes and then offered an explanation.

MR. HESTER: I don't think -- Your Honor, she's not explaining the question I asked her.

THE COURT: Right. The answer was non-responsive. I'll strike it.

BY MR. HESTER:

Q. Dr. Keyes, I just wanted to ask about this sentence that says, "Of these prescriptions, 65 percent were for short-term therapy of less than three weeks."

Do you see that?

A. I do.

Q. And does that accord with your understanding that, in this time frame of 2014, 65 percent of the opioid prescriptions written in the country were for a duration of less than three weeks?

A. Yes, that is my understanding.

Q. Also on the same page, it goes on to say that, "Chronic pain not caused by cancer is among the most prevalent and debilitating medical conditions, but also among the most controversial and complex to manage."

Do you see that?

A. I don't. I'm sorry. It's on the first page?

Q. It's actually the first sentence of the whole article.

A. Oh.

Q. Didn't mean to trick you there. So, yeah, just so -- the article begins that way.

Do you see that?

A. Yes.

Q. That's a true statement, correct?

A. I think that -- I don't know -- I have not reviewed the literature on what the most prevalent and debilitating medical conditions would be. I actually might -- I might have my own views on that.

Certainly, I would agree that chronic pain not caused by cancer is prevalent and is a challenge to clinically manage. I don't know that I would agree that it is the most prevalent.

Q. Do you agree that chronic pain not caused by cancer is a debilitating medical condition?

A. I agree that chronic pain not caused by cancer is a debilitating medical condition.

Q. And do you see -- do you see further down on this same first page, toward the bottom of the page, there's a statement that says, "The major source of diverted opioids is physician prescriptions?"

Do you see that?

A. Oh, I'm sorry. We're in a different section? Okay.

Q. Yeah, sorry. It's the last full paragraph on the page. States, "The major source of diverted opioids is physician prescriptions."

Do you see that?

A. I'm just trying to find it.

Q. It --

A. Yes. I see that.

Q. And that's a true statement, correct?

A. I mean, if I -- I would say a major source of diverted opioids is physician prescriptions. I think there are other major sources, but physician prescriptions is certainly a major source of diverted opioids.

Q. Let me ask you to look at Page 4, please. There's -- over on the left-hand side, first full sentence on the page, there's a reference -- well, I guess I should actually begin by pointing you to the prior page, Page 3, and there's a sentence on the right-hand side. "The repeated administration of any opioid almost inevitably results in the development of tolerance and physical dependence."

Do you see that?

A. Yes.

Q. And then it goes on to say over on Page 4, "These short-term results of repeated opioid administration revolve -- resolve rapidly after discontinuation of the opioid."

Do you see that?

A. Yes. They're referring to the intracellular signaling cascades.

Q. And that accords with your understanding, correct?

A. I'm sorry. What -- I don't understand the question. Whether intracellular signaling cascades resolve?

Q. When Dr. Volkow here says, "These short-term results of repeated opioid administration resolve rapidly after discontinuation of the opioid," that's a true statement, correct?

A. There's a sentence in between the two that we haven't discussed that I think is important for contextualizing the short-term results of -- when she says "these short-term results", she's referring to the predictable phenomenon reflect contra-adaptations in opioid receptors and their intracellular signaling cascades. So, that's what's referred to as "these short-term results".

Q. And it accords with your understanding that those results resolve rapidly after discontinuation of the opioid?

A. The intracellular signaling cascades, yes.

Q. Then, over on the right-hand side on Page 4, the last full paragraph on the right-hand side says, "Unlike tolerance and physical dependence, addiction is not a predictable result of opioid prescribing."

Do you see that?

A. I see that.

Q. And then it goes on to say, "Addiction occurs in only a small percentage of persons who are exposed to opioids."

Do you see that?

A. I do.

Q. And did you -- that's your understanding of what Dr. Volkow -- how Dr. Volkow has characterized addiction risks here?

A. I -- I agree that a small percentage of people who use opioids develop Opioid Use Disorder and I think that's what she's saying. I think you have to contextualize that with the amount of opioid prescribing as we do in public health.

Q. But so, you would agree with the statement she makes here?

A. Yes. There's numerous studies in the report that demonstrate the same statement.

Q. Let me ask you to look over on the next page, Page 5, please. And in the first full column on the left side there's a sentence that begins, "However, we do know that the risk of opioid addiction varies substantially among persons, that genetic vulnerability accounts for at least 35 to 40 percent of the risk associated with addiction."

Do you see that?

A. I do.

Q. And does that accord with your understanding that

genetic vulnerability accounts for at least 35 to 40 percent of the risk associated with addiction?

A. Yes.

Q. Okay. Dr. Keyes, we can put that one down for a minute.

I want to turn back to discuss your testimony and the estimates on the number of deaths caused by prescription opioids in Huntington and Cabell County. So, just to set the table here, you're not a Medical Examiner, correct?

A. Correct.

Q. And to estimate deaths attributable to prescription opioids, you relied on data compiled by the CDC from death certificates, correct?

A. That's right.

Q. And the CDC data is based on death certificates prepared by authorities in each jurisdiction where the deaths occurred, correct?

A. Yes.

Q. You did not look yourself at the underlying death certificates, right?

A. That's right.

Q. But you are aware that there are circumstances where more than one drug will be listed in a death certificate, correct?

A. Yes.

Q. And, in fact, in Huntington-Cabell, there are many polydrug overdoses, meaning overdoses where multiple drugs are found in somebody's body at the time of death, right?

A. That's right.

Q. And so, for purposes of your calculations, if prescription opioids were one of the drugs listed in the CDC data, you directly contribute that death to prescription opioids even if there were other drugs also identified as contributing to the death, correct?

A. That is the reliable methodology of my field.

Q. But let me make sure I understand what you did. I didn't ask whether it was reliable. I asked what you did.

A. Okay.

Q. And what you did was if a prescription opioid was one of the drugs listed in the CDC data as contributing to death, you directly attributed that death to prescription opioids even if there were also other drugs also listed as contributing to the death, correct?

A. Of course, yes, I did.

Q. So, if you have a death certificate that lists both prescription opioids and heroin, the death certificate would be coded in the CDC data as involving both prescription opioids and heroin and you attribute that death directly to prescription opioids?

A. Yes. And I can explain the reasoning why, if that

would be --

Q. I'll drill into that more later, but for now, I'm just trying to set the table on what you did.

A. Okay.

Q. And, in fact, there could be circumstances where four or five drugs would be listed on the death certificate as contributing to the death and if one of them is a prescription opioid, you would attribute that death directly to prescription opioids?

A. Absolutely.

Q. So, to be clear, some portion of the deaths that you categorize as directly attributable to prescription opioids were coded by the Medical Examiner as also involving heroin or illicit fentanyl?

A. Yes.

Q. And you don't actually know how many, correct?

A. In Cabell County or in West Virginia?

Q. In Cabell County?

A. You're asking if I know how many deaths had fentanyl -- had prescription opioids without one of these other codes?

Q. No. I was going at it the other way. So, if you had a death certificate that listed prescription opioids, and heroin, and fentanyl, all three were listed as contributing to the death, I'm asking, you don't know how many of those there were?

A. I think we do know that in the CDC data. I could -- we -- we know it for -- I guess at the county level there might not be sufficient numbers to estimate that directly.

Q. So, I mean, just to be clear on the methodology, you could have a circumstance where there might be multiple drugs listed, along with prescription opioids, that you attribute that death directly to prescription opioids and you don't know how many of those deaths there were that might list multiple drugs alongside the prescription opioids?

A. I think we do know how many list multiple drugs.

Q. For purposes of your death estimates in Cabell-Huntington?

A. Oh, I -- is that knowledge knowable? Yes. But was it relied upon for my methodology? No.

Q. Okay. So, just to make sure --

A. I apologize. I was not --

Q. No. Just so we're communicating here. So -- so, for purposes of your analysis in Cabell-Huntington, when you were attributing deaths to prescription opioids, you didn't undertake to analyze how many of the deaths that you directly attributed to prescription opioids also listed other drugs as contributing to the death?

A. That was not part of the methodology.

Q. And so, you didn't do that?

A. I didn't -- it's not part of the methodology. I may have done it -- I might have looked at that in developing the methodology, but it's not part of the final number that I derived.

Q. And so, we couldn't go back and figure that out from the work you did?

A. No.

Q. And so, some portions of the death that you categorized as directly attributable to prescription opioids also were coded by the Medical Examiner as involving cocaine, for instance?

A. Yes.

Q. You don't know how many were coded that way?

A. Off the top of my head, sitting here today, I don't, but I don't believe that information is obtainable.

Q. But it wasn't part of your methodology?

A. No.

Q. And you also attribute a certain number of illicit opioid deaths indirectly to prescription opioids, correct?

A. That's right.

Q. So, where you have a death where the soul cause is listed as fentanyl on the death certificate, you indirectly attribute a percentage of those deaths to prescription opioids?

A. That's right.

Q. And this is based on your assumption of a gateway that you discussed last week, correct?

A. Yes.

Q. So, I'm going to come back to that later, but I just wanted to put a pin in it that that's the basis by which you do this indirect attribution, correct?

A. Yes he.

Q. The NSDUH data, the government data, was your basis for estimating deaths indirectly attributable to prescription opioids, correct?

A. That's right.

Q. And the NSDUH data is limited to people who misused -- misused prescription opioids prior to heroin use, correct?

A. That's right.

Q. And so, with respect to the NSDUH data on prescription opioid misuse, you don't know what percentage of those people actually had a prescription for opioids, right?

A. Certainly, that is estimate-able [sic], and that's the methodology I outline in the report, that there is this quite large overlap. Most non-medical users also have a prescription at some point in their lives.

Q. But you -- you don't know what percentage that is? That wasn't something you developed as part of your methodology, correct?

A. For the indirect attribution percentage, I used the

proportion of heroin users who started with non-medical opioid use.

Q. And so, to be clear, the deaths that you're attributing indirectly to prescription opioids did not have a prescription opioid coded in the CDC data, correct?

A. The people I am indirectly attributing to prescription opioids did not have a prescription opioid as a contributing cause at the time of death.

Q. So -- so, the death certificate coded by the CDC doesn't have prescription opioid listed as a contributing cause of death in the ones that you indirectly attribute to prescription opioids?

A. That's right.

Q. And when the death certificate does not list prescription opioids as a contributing cause of death, the Medical Examiner concluded that prescription opioids were not a source of the death, correct?

A. A proximal cause of the death. It did not contribute to the death as it occurred.

Q. So, when we have this indirect attribution, those all involve death certificates where the Medical Examiner coded the death as caused only by either heroin or illicit fentanyl, correct?

A. Right. And I can provide a little bit of context for that, if that would be helpful.

Q. I -- for right now, I'm just trying to set the stage on what you did. And I've got that correctly, right?

A. That's correct. That's the methodology.

Q. And you've not examined the drug use histories of any of the individuals whose opioid overdose deaths you count as indirectly attributable to prescription opioids to determine whether they ever used prescription opioids, correct?

A. It's an estimate based on the literature, so I did not look at any particular death and their drug use history.

Q. So, let's take a step back and talk about how you developed your report. You served your expert report on August 3, 2020, correct?

A. Yes.

Q. You then served an errata three weeks later on August 24, correct?

A. That's right.

Q. You were then deposed on September 15, correct?

A. Yes.

Q. And then you served a second errata a week after your deposition on September 23, correct?

A. That's right.

Q. And between your report and the two errata, your calculations on these death numbers changed, correct?

A. Yes.

Q. In your original report you estimated the number of

deaths directly and indirectly attributable to prescription opioids using the methodology we just reviewed, you did a direct attribution and an indirect attribution, correct?

A. Yes.

Q. And, in your original report, you reported that of the 105 opioid overdose deaths in Cabell-Huntington in 2018, 104 were directly attributable to prescription opioids, right?

A. Is the figure that's in the report in front of me based on the original or the revised? I just want to make sure that I'm giving you --

Q. I think what we have handed you is your original report.

A. And do you have the revised that I can compare it to?

Q. Yes. We can try to come up with those. It may take us just a minute, please.

A. Sure.

Q. Let me ask you before we -- before we get you the documents, do you remember that you had to change the number from what you had in your original report? You had to revise it downward?

A. Well, there was two -- one, I had a typo and that was -- I corrected it. And then, secondly, I also revised the estimation. Could I have both?

MR. HESTER: May I approach, Your Honor?

THE COURT: You may.

MR. HESTER: I think if it's okay by counsel, this was just to refresh Dr. Keyes' recollection. I wasn't planning to introduce this as an exhibit.

THE COURT: You're refreshing her recollection on the errata?

MR. HESTER: Yes.

BY MR. HESTER:

Q. Dr. Keyes, as I understand it, it would help you to have the errata to refresh your recollection on the sequence of events?

A. Yes.

THE COURT: You don't remember independently the sequence of events?

THE WITNESS: I -- I remember this -- I just -- he asked, well, the number was 105. And then, it was 104. And then you arrived at -- I just don't remember the exact numbers, but I remember the sequence of events.

BY MR. HESTER:

Q. So, Dr. Keyes, let me hand you two errata. And the first errata that was submitted on August 24 and the second errata from September 23, those will help refresh your memory on the sequence?

A. They will. I'm sorry.

MR. HESTER: Your Honor, may I approach?

MR. ACKERMAN: Your Honor, may we get copies,

please?

MR. HESTER: Sure. Sorry.

BY MR. HESTER:

Q. So, Dr. Keyes, I think the first question I had for you was in your original report you reported that of the 105 opioid overdose deaths in Cabell-Huntington in 2018, 104 were directly attributable to prescription opioids; is that right?

A. That's right.

Q. And then that was an error? I think you've said that was a mistake?

A. Well, not exactly. I can explain, if that's helpful.

Q. Well, you had counted every single death involving fentanyl as a prescription opioid death?

A. So, that was the CDC's guidance. We followed the CDC's guidance on categorizing prescription opioids. And then, I decided that I was -- that that wasn't the best guidance to use because the T40.4 deaths, which are the synthetic opioid deaths, would include illicit fentanyl.

And so, I thought, well, I don't want to include that as a prescription opioid because a lot of it might be illicit. And so, that's why I made that revision. It went from what the CDC recommends in terms of categorizing prescription opioids to what I felt was a more accurate reflection, which would be not including all of those as

prescription opioids because every fentanyl death is not a prescription fentanyl death, to -- just to provide the context there.

Q. So, you concluded that the first numbers weren't correct, right?

A. Well, the first numbers are what the CDC recommends that we do and I decided that that wasn't the best label. To call those all prescription opioid deaths was probably not the best way to estimate the direct attribution of prescription opioids.

Q. Well, let's just make sure we got the context. You started with 104 deaths that you directly attributed to prescription opioids, correct?

A. That's right.

Q. Then you dropped the number that you directly attributed to prescription down to 32, correct?

A. That's right.

Q. And then you dropped the number again to 20 and --

A. Yes, and I can explain. Okay, sorry.

Q. Dropped the number --

A. I'm excited about methods. I've got to --

Q. You dropped the -- you dropped the number again to 20 deaths attributable to prescription opioids in your second errata, correct?

A. That's right.

Q. So, we went from 104 deaths directly attributable to prescription opioids and in the original report down to 32 down to 20 deaths directly attributable to prescription opioids, correct?

A. That's right.

Q. And let me ask you to look in particular at your second errata. And this comes up with a number of -- as we've discussed, 20 deaths that you attribute directly to prescription opioids, right?

A. That's right.

Q. And that's based on the methodology that we discussed a few minutes ago, correct?

A. If I could just qualify one part of what you're saying that I'm realizing is a little bit inaccurate, is that you're just talking about the 2018 deaths and that's where the fentanyl issue becomes really apparent. Everything before 2015, there really aren't any changes. It was just when fentanyl happened that we had to change the methodology to reflect the epidemiological situation.

So, not all of the numbers decreased in terms of the direct attribution to prescription opioids, especially those pre-2015 numbers. There really weren't any changes.

Q. Fair enough. So, I'm focusing -- I am focusing principally on 2018 because 2018 is the number that ultimately gets supplied to Dr. Alexander for purposes of

his abatement report, correct?

A. I don't know what --

Q. You don't know what's happened with the numbers you've estimated?

A. I know that various other experts have relied upon them, but I haven't -- I have tried to stay out of that.

Q. Okay. So, but in any event, I am -- it is fair I'm focusing on 2018. And so, I want it to just be clear in the record that it went from 2018 you started at 104 deaths directly attributable to prescription opioids. You then dropped the number to 32 deaths directly attributable to prescription opioids. And then you dropped the number again to 20 deaths directly attributable to prescription opioids in 2018, correct?

A. That's right.

Q. And then you attribute 45 other deaths indirectly to prescription opioids, correct?

A. Yes. The number went up. If we're talking about the trajectory of indirectly and directly attributable. Because the number of directly attributable went down, the number indirectly attributable went up. There's kind of a -- a correspondence between those two.

Q. So, again, just focusing on the 2018 numbers here, the -- just so we have it for the record and it's clear, the -- you've indirectly attributed 45 overdose deaths to

prescription opioids based on the indirect attribution methodology we discussed a few minutes ago, correct?

A. That's right.

Q. And the total number of deaths that you've analyzed is 105, correct? Those are the deaths for opioid overdoses in 2018, correct?

A. That's right.

Q. So, this means, applying your methodology, that you attribute directly approximately 20 percent of the opioid-involved deaths in 2018 to prescription opioids, correct?

A. You're saying it would be whatever 20 plus 45 divided by 105?

Q. Well, no. I was really focusing on the 21st, just so the record is clear.

A. Oh.

Q. So, there's 105 opioid-related overdose deaths in 2018 in Huntington-Cabell that you've analyzed, right?

A. That's right.

Q. And of those 105, there are 20 that you directly attribute to prescription opioids, correct?

A. That's correct.

Q. And that's based on the direct attribution methodology we discussed a few minutes ago, correct?

A. Uh-huh, yes.

Q. And so then, in addition to those 20, there's another 45 deaths that you attribute indirectly to prescription opioids?

A. Yes.

Q. Based on the methodology we discussed a few minutes ago; is that right?

A. That's right.

Q. And so, from the 105 total deaths, total opioid-related overdose deaths in 2018, we're left with, I believe, it's 40 deaths that you don't attribute either directly or indirectly to prescription opioids, correct?

A. Just about, yeah.

Q. So, that means you have a -- you have a 40 percent or so of the 105 total opioid-related overdose deaths you don't attribute to prescription opioids, correct?

A. That's right.

Q. Either directly or indirectly, correct?

A. Yes.

Q. Did you say yes? I'm sorry.

A. Yes.

THE COURT: We need to pull the plug here, Mr. Hester, when you get to a convenient stopping place.

MR. HESTER: All right. This is -- this is as good a time as any, Your Honor.

THE COURT: All right. We'll come back at 2:00

and you can get up and walk around or do whatever you want to do for two hours, Dr. Keyes.

THE WITNESS: Thank you.

(Recess taken)

THE COURT: Is Dr. Keyes in the courtroom?

Okay, Mr. Hester, you may continue, sir.

MR. HESTER: Thank you, Your Honor.

BY MR. HESTER:

Q. Good afternoon Dr. Keyes.

A. Good afternoon.

Q. Earlier today, you made a reference to pill mills; do you recall that?

A. Yes.

Q. And I wanted to ask you in your report that you submitted, your expert report that you submitted in the MDL litigation, you stated that, quote, "Pill mills do not explain in any significant way the expansion of opioid prescribing and opioid-related harm in the U. S."

Do you recall saying that in your MDL report?

A. I do.

Q. And that's a true statement, correct?

A. Yes.

Q. Let me turn now to your estimate of the OUD population in Huntington and Cabell County. And I'm going to do a little bit on the board here.

And your view, Dr. Keyes, is that there is no systematic way to count the OUD population, correct?

A. That's right.

Q. And so, because you can't actually count the OUD population, you developed an estimate for it, correct?

A. Yes.

Q. And to estimate it, you divided the number of overdose -- overdose deaths due to drugs in Cabell-Huntington in 2018 by a mortality rate; is that right?

A. By two mortality rates.

Q. Right. So, I will get into that.

A. Okay.

Q. And maybe we'll start with the simpler point first.

You -- you refer to a methodology that you described as a multiplier method, right?

A. Yes.

Q. And if I can write this formula over here, I will ask you, Dr. Keyes, so we're talking the same language, I hope. So, the basic principle of the multiplier method is that if you know the number of deaths due to drug overdose and you know the mortality rate associated with a population of drug users, you can back into the OUD number; is that right?

A. That's the basic idea.

Q. So, another way to put that based on the formula I put up there, you could also multiply OUD, the OUD population,

by a mortality rate and that would give you a number of deaths, right?

A. That's right.

Q. But, of course, in this case, we don't know the OUD population, so you observe the number of deaths and then you come up with a mortality rate and that's the way you estimate OUD population, correct?

A. Well, not exactly because, as I discussed on Friday, there were a number of adjustments that you need to make up epidemiologically based on the current state of the epidemic.

Q. So, but in the simple model -- and I'm going to get into the adjustments.

A. Okay.

Q. But in the simple model, if you know the number of deaths and you know a mortality rate, you can back into an OUD population, correct?

A. That's right.

Q. So, you need to know two numbers. You need to know a death number, which is due to drug overdoses, correct?

A. The number I used was deaths due to drug overdose.

Q. And then the other number would be the mortality rate associated with the population of people who have OUD, correct? Those are the two things you're trying to get to?

A. Generally, although there's not one mortality rate

because of -- I know we're going to get into it. I just want to make sure that, for the record, it's stated the way that I did it, which is that I used two mortality rates.

Q. Right. So, let's talk about the numbers you used but, first, I wanted to be clear that because you're estimating an OUD population, the accuracy of the death number and the accuracy of the mortality number is extremely important to coming up with an accurate OUD number, right?

A. Yes.

Q. And if either -- if you're off on the deaths or if you're off on the mortality rate, you may be off on your OUD estimate, correct?

A. Not exactly. The bioses would need to be working in different directions in order for the OUD to be mis-estimated. So, you could mis-estimate one, but as long as you're mis-estimating the other in a similar direction, then your OUD estimate may still be unbiased.

Q. Well, maybe I can take it more concretely in this case. You came up with a specific number of deaths, so you know that number that you have come up with, right, based on the CDC data?

A. Yes.

Q. So, in the circumstance where you have a fixed number for deaths, the question is, is your mortality rate accurate, right? That's going to be the driver of the

accuracy, the OUD number, right?

A. Well, again, I mean, it would depend on if there's any -- if there's any mis-classification of death, for example, as long as that mis-classification is consistent in the mortality at rate that you've estimated, then your OUD rate would be unbiased.

So, I wouldn't agree with that as a blanket statement, although there could be situations in which one or the other estimate would -- would lead to a biased estimate of OUD.

Q. In this case, you came up with a number of 115 for deaths; is that right?

A. Do you know what page that's on?

Q. 42 of your report, I think.

A. Okay. 115, yes.

Q. Right. So, let's drill into that 115 just a little bit. Before lunch, we were talking about the fact that you had looked at -- you had come up with a number of 105 opioid-related overdoses, correct?

A. That's right.

Q. For this calculation, to do your OUD estimate, you used the number 115, correct?

A. Correct.

Q. So, you added ten more drug overdose deaths that were not due to opioids, correct?

A. Well, I don't think that those two should be equated in

any way because this method relies on the all drug overdose death number, not the opioid overdose death number. So, I didn't add them. There happened to be 115 all drug overdose deaths, of which 105 were opioid-related.

Q. Okay. So -- so, maybe I'll just put it the other way around. In this 115, there are overdoses for non-opioid drugs, correct?

A. That's right. That's what the method required.

Q. And so --

A. And I -- I can explain that, if you'd like.

Q. Well, let me walk through it and I think we'll get to the right place. So, the 115 is going to include both opioid-related deaths, but also drug overdose deaths due to, for instance, methamphetamine or cocaine, correct?

A. Exactly.

Q. And so, it's going to include deaths caused by methamphetamine, for instance, even if there was no opioid involved at all?

A. And that's because the metaanalysis that it relies on required that the OUD mortality rate be applied to the all drug overdose category.

Q. But I just want to make sure that the method is clear. You estimated or you came up with a count of 105 deaths that are opioid-related, correct?

A. Right.

Q. And of those 105 that are opioid-related, we discussed before lunch that there were 20 directly attributed to prescription opioids under the method we discussed earlier, correct?

A. Yes.

Q. And there are 45 that you attribute indirectly to prescription opioids under the methodology we discussed before, correct?

A. That's a different estimation process from this number but, yes, in a different section of the report when I estimate the attribution, that's what was --

Q. So, when we look at the 115, the number that you used for this OUD calculation, it means that 50 of the 115 deaths are not attributed by you either directly or indirectly to prescription opioids, correct?

A. I haven't done that calculation. That was for -- I haven't -- I haven't estimated out of the 115 the number that would be indirectly attributable to prescription opioids. Certainly, additional -- if you added the additional overdose deaths, there would be a different calculation for how many of them are indirectly attributable to prescription opioids. So, it wouldn't be 50.

Q. Well, you have a number of 105. Are you saying there's some different number that you haven't calculated for the number of deaths attributable to --

A. No. I'm saying that if I were to calculate the number of deaths that were attributable -- directly and indirectly attributable to prescription opioids based on the 115, it would be a different number than the number that I based directly and indirectly attributable to prescription opioids based on the 105.

Q. Do you have any reason to think that within this 115 death count that you used that there's more prescription opioid deaths attributable than there was in the 105 we discussed earlier when you went through the opioid-related deaths?

A. Indirectly attributable, yes.

Q. Indirectly? So, you would say that there are some that you would view as indirectly attributable in this 115, but you haven't done that calculation?

A. I haven't -- yeah. I'm saying that hypothetically I would have to do a different analysis to answer your question, which I have not done, because these are all drug overdose deaths including, you know, everything.

Q. Right. So, this 115 includes drug overdose deaths that don't involve opioids at all?

A. Correct.

Q. So then, for the mortality rate, you relied on an analysis that was published in 2019 in a journal called JAMA Psychiatry, right?

A. That's right.

Q. So, let's take a look at that study.

MR. HESTER: May I approach, Your Honor?

THE COURT: Yes.

THE WITNESS: Did you also print out the supplemental material because it's Figure 7-20 of the supplemental material that I relied on for the death rate. And so, that's a very important part of this discussion.

MR. HESTER: Let's try to see if we can straighten it out.

THE WITNESS: Okay.

MR. HESTER: I'll do my best.

BY MR. HESTER:

Q. So, Dr. Keyes, we've handed you a document marked DEF-WV Exhibit 2495. It has the title All-Cause and Cause-Specific Mortality Among People Using Extramedical Opioids, a Systematic Review and Metaanalysis.

Do you see that?

A. I do.

Q. And is this the paper that you relied on for the mortality rate that you used to do the OUD estimate?

A. There were two mortality rates. One of them anchor -- well, both anchored in this paper, but one was -- I relied on other information, as well.

Q. Right. So -- so in -- let's just be clear on this.

This is what you call the Larney study, right?

A. That's right.

Q. And it's called a metaanalysis because it analyzes the results from other studies, right?

A. A metaanalysis takes a lot of studies and comes up with a summary of all of those studies.

Q. And so, the Larney metaanalysis, if you look -- if you look over at Page 4 of this paper under drug-related deaths, there's a statement, "Across the three definitions for which data were extracted, the pooled CMR was 0.52 per 100 per person-years."

Do you see that?

A. I do.

Q. And that's one of the mortality rates that you used to calculate OUD?

A. That's correct.

Q. So, let's put that on the board so we don't lose track of it. So, I've written Larney = .0052. That's a correct transition from the numbers in the report, right?

A. That's right.

Q. And so, the goal of this Larney study was to estimate the mortality rate in people who engage in non-medical opioid use; is that right?

A. Yes.

Q. And so, the rate that you used, this rate I've put up

of .0052, the rate that you used for your calculation is the rate at which people using extra-medical opioids suffer drug-related overdose deaths, not just opioid overdoses?

A. Sorry. I -- there is one correction I need to make to your statement.

Q. Okay.

A. Which is that if you look at Figure 7-20 in the supplemental materials, I went through each of the different -- I think it's 56 different cohorts that informed that death rate calculation to ensure that the majority of people had OUD and not extra-medical opioid use.

Q. Well, okay, but --

A. And you -- you had said extra-medical opioid use, but it's really OUD.

Q. Well, okay. Maybe -- maybe I can clean that up. So, the Larney study includes people who did not have OUD, correct? It includes mortality rates for people who did not have OUD, correct?

A. I don't know what you mean.

Q. Let me point you to Page 2 of the document under the heading for Inclusion and Exclusion Criteria.

Do you see that, right-hand column?

A. Sorry. Hold on.

Q. Page 2.

A. Yes.

Q. Are you with me there? And there's -- there's a third sentence that says, "Cohorts did not need to be opioid dependent or have Opioid Use Disorder to be included."

Do you see that?

A. I see that.

Q. And so, just -- I think your point is you looked at this?

A. Right.

Q. I wanted to make sure I understand the Larney design included studies of people who had overdoses who did not have OUD, correct?

A. I suppose it's possible, but in the studies that I used for my metaanalysis estimate for my OUD calculation, I made sure to go through the studies to make sure that I wasn't -- that I was appropriately capturing my target population.

Q. Well, you didn't change the Larney number. You used the Larney number as written in the paper, correct?

A. Right, which if you go to Figure 7-20 and you look at those cohort studies, I think you'll see that they include people who are in treatment for opioid dependence.

MR. HESTER: Your Honor, the witness is raising a new point that was not disclosed in her expert report. I do not believe this point has ever been made to us previously. I mean, I can press on because I think I can get through this, but I -- just for the record -- I believe this is not

something that Dr. Keyes stated in her report.

THE COURT: Well --

MR. HESTER: I'll -- I'll press on, Your Honor. I'm not asking you to do anything.

THE COURT: Mr. Farrell, do you want to say something?

MR. FARRELL: Well, the fact that this wasn't asked before doesn't make it untrue.

THE COURT: Yes. It was in response to one of your questions, Mr. Hester. So, you can go ahead.

MR. HESTER: Well, I would only say, Your Honor, the expert, in my view, has an obligation to disclose her methodology. This is complicated.

THE COURT: Well, that's true.

MR. HESTER: And it's going to get a little more so as we work through it. And so, the fact that this is a new piece of the methodology that wasn't disclosed, I must say, is a little bit of a curve ball for us.

THE WITNESS: I'm sorry. It's not a new piece. I -- I -- I can contextualize it further, but it's not a new piece of methodology. It's all in the report.

MR. HESTER: I'll press on. I just wanted to preserve my point.

BY MR. HESTER:

Q. So, Dr. Keyes, you recognized that the Larney study was

not enough or was not the only thing you could use for the mortality rate, correct, because you recognized that there is a fentanyl adjustment you needed to make, correct?

A. Yes.

Q. And so, let's just put that formula up on the board for just a minute. So, you actually broke the mortality rate in half -- or into two parts, not in half, but you broke it into two parts.

So, you did OUD as a function of 115, which was your death number, divided by a prescription opioid mortality rate based on Larney?

A. Well, it's not a prescription opioid mortality rate.

Q. Okay. Or mortality -- what would be more accurate?

A. It would be --

Q. Larney?

A. Right. It would be the mortality rate for -- I suppose I would -- I would characterize it as the OUD overdose mortality rate for an -- aggregated across non-fentanyl opioids. That's probably hard to write out.

Q. Do you have a clever way for me to abbreviate that?

A. Non-fentanyl.

Q. Okay.

A. Non-fentanyl.

Q. What if I put "NF"?

A. Sure.

Q. So, you broke it into two mortality rates, one associated with non-fentanyl, and the other associated with fentanyl?

A. That's right.

Q. Right? And then you made a determination that there was a percentage breakdown in the deaths in 2018, correct?

A. Well, if I could just describe the methodology in a little more detail. I took the two overdose death rates and then I weighted them by the proportion of deaths by year for which T40.4 or synthetic opioids were a contributing cause. And so, in 2018, I'm sure you have the number with you. It's probably 80-something percent, right?

Q. 84 percent.

A. Right.

Q. Does that sound right?

A. That sounds about right. And so, in previous years it was lower, and then it increased over the course of the OUD yearly estimation that I did.

Q. So, let's put that up on the board just so we don't lose that. So, you had an 84 percent. Those were the deaths that you construed as attributable to synthetic opioids, correct, that percentage?

A. 84 percent of overdose deaths in 2018 were coded with a T40.4 code, which is the synthetic opioid code.

Q. So, you concluded that, as you're looking at this 115

number, you would view 84 percent of those deaths as due to synthetic opioids?

A. Yes. They had synthetic opioids as a contributing cause.

Q. Well, and you viewed that as the contributing cause for 84 percent of the deaths, correct?

A. A contributing cause. There might have been other drugs listed on the death certificate.

Q. But not prescription opioids, correct?

A. Prescription opioids could have been listed on the death certificate.

Q. Well, but you weren't attributing these to prescription opioids.

A. That was a different analysis. So, in this analysis, I'm weighting the death rate, the OUD death rate for fentanyl, by the proportion of deaths that had a fentanyl -- had T40.4 as an underlying cause.

They could have T40.1, T40.2, T40.-infinity, but they at least had T40.4.

Q. So, I'm with you. So -- so, you're saying that you viewed, from among this 115 deaths, 84 percent of them you've had synthetic opioids listed as a cause?

A. That's right.

Q. So, that left 16 percent for non-fentanyl; is that right?

THE COURT: Is synthetic opioid equivalent to fentanyl or is there a difference? I'm a little bit confused here.

THE WITNESS: There's a -- I can answer or --

MR. HESTER: Yes, please.

BY MR. HESTER:

Q. So, Dr. Keyes, synthetic opioids, that phraseology is typically applied to illicit fentanyl, correct?

A. It's applied to any fully synthetic opioid. Fentanyl would be one of which there's prescription varieties and illicit varieties, but there's many other kinds of synthetic opioids, as well.

Q. But, Dr. Keyes, just to be clear, the opioids that you're focusing on here, these are -- these are illicit fentanyl deaths, correct?

A. Well, that's another discussion that we should probably have about the proportion of those that are prescription fentanyl versus illicit, which I also provided an estimate of. I'm sure we'll -- we'll get there.

Q. Sorry. You understood that the vast majority of this 84 percent of fentanyl deaths were illicit fentanyl, correct?

A. Yes.

Q. And you attributed, in fact, three deaths out of 115 to prescription fentanyl, correct?

A. That's right.

Q. So, if I do the math, and I'm not fast enough to do it in my head, but it would be 84 percent times 115 would be the fentanyl deaths. And then we would subtract 3 from that to figure out how many you viewed as prescription fentanyl, correct?

A. That seems reasonable.

Q. And putting it the other way around, therefore, if we wanted to figure out how many were illicit fentanyl, it would be 84 percent times the 115. And then, you would subtract 3 from that for the prescription fentanyl deaths, correct?

A. That's right.

Q. So, if we -- and as we discussed before, for the non-fentanyl, you used Larney as your multiplier number, correct?

A. Yes.

Q. And so that the math doesn't even get more complicated, I'm going to ask you to help me. I've even got a calculator here, Dr. Keyes.

MR. HESTER: Can I approach, Your Honor?

THE COURT: Yes.

BY MR. HESTER:

Q. And so, Dr. Keyes, we know that we're applying the Larney number .0052 to the 16 percent that are non-fentanyl,

correct?

A. That's -- well, it's -- I think that's one way to phrase it. It weights the denominator.

Q. Right.

A. By the -- it's .0052 times 16 percent.

Q. And maybe just to put it up here in the corner, I don't want to do too much with it, but the point is, that you're making is, it's .84 times your fentanyl mortality rate plus .16 times the non-fentanyl?

A. Yes. That sounds about right.

Q. That's what -- that's what we need to come up with here to do the proper weighting because we've got a non-fentanyl mortality rate and a fentanyl and we need to weight them, correct?

A. That's right.

Q. And sorry this is a little messy. But I think, if you can help me with this, Dr. Keyes, we know -- we know the Larney number. We know the .0052. And we know that -- the 16 percent. So, we can come up with what the NF number is, correct? If you multiply -- if you multiply .1 --

A. Yes. We could come up with the NF number, yeah.

Q. Come up with that number --

A. Yes, because that would --

Q. You check -- check me. I think the weighted number is .000832.

A. That's what I get, as well.

Q. Okay. So, we're going to do a little more math here. Or maybe this is Algebra. So, its OUD is going to be 115 divided by .00832. That's the number you came up with, right?

A. Yes.

Q. Oh, I'm sorry. I'm sorry, Dr. Keyes. I think I dropped a digit. It should be .000832, right?

A. I already cleared it on my calculator, but --

Q. Can you do that again?

A. Sure. .0052 times -- 000832.

Q. Okay. And that -- so, that .000832, that represents the weighted mortality rate for the non-fentanyl overdoses, correct?

A. Yes.

Q. And then you needed a different mortality rate for the fentanyl overdoses, correct?

A. That's right.

Q. And so, I'm just going to keep an "F" here for now and we'll run through how you did that. Because the fentanyl adjustment was what you needed to do, you couldn't use just the straight Larney number; you had to adjust the Larney number?

A. That's what I decided to do, yes.

Q. And for that purpose, you took the CDC data on overdose

deaths between 2011 and 2015; is that right?

A. That's right.

Q. And do you -- do you have handy in your report the CDC overdose data or would it help you if I provided you with those?

A. There's one specific article that I thought had a nice figure. I'm sure you have it. I think --

Q. Is that the Hedegaard article?

A. Sounds right, but if you have the overdose death rate from those years, we could --

Q. Yes. We can -- I think we can do that most effectively.

MR. HESTER: May I approach, Your Honor?

BY MR. HESTER:

Q. Dr. Keyes, we've handed you two documents. They're marked sequentially. And let me explain them just a little bit and then I'll ask you to confirm that this looks right to you.

There's DEF-WV 2586 headed Drug Overdose Deaths in the United States, 1999-2018 written by Holly Hedegaard and others.

Then there's DEF-WV 2587, which I can represent to you is the appendix that goes along with the article --

A. Excuse me. Those articles are not referenced in the report on that page.

Q. Yeah. I --

A. It's the Dowell article.

Q. I will -- are -- let me ask you if these -- so, Dr. Keyes, are you familiar with these data briefs that are published by the CDC?

A. I am.

Q. And I wanted to -- I think we can get to the same place with this article.

A. I don't think so because I believe the Dowell article -- these are for all drug overdose deaths and the Dowell article, I believe, is opioid overdose deaths.

Q. Okay. Well, let me try that.

A. Okay.

MR. HESTER: May I approach, Your Honor?

THE WITNESS: Thank you.

MR. HESTER: Sure.

BY MR. HESTER:

Q. So, Dr. Keyes, are you able to -- well, maybe let me set the table just a little bit more. You looked at CDC mortality data to come up with your fentanyl adjustment; is that right?

A. I did.

Q. And are you saying that the Dowell document is where you found the CDC data?

A. Yes. The figure that is in Dowell for illicit opioid

overdose deaths from 1999 to 2015.

Q. So, you're looking -- maybe I should back up. I'm sorry. I didn't set the record properly.

We've handed you DEF-WV Exhibit 2497 headed Underlying Factors in Drug Overdose Deaths and, Dr. Keyes, this is the document you were referring to just a minute ago, the Dowell article?

A. Yes.

Q. And you were looking at the -- at the CDC -- at the CDC data shown on Page 4 of this document?

A. Yes.

Q. And can you tell me which of the charts you used for the CDC data?

A. If you look at the illicit opioid overdose death, which is the top figure on Page 4.

Q. Yes.

A. And you compare the overdose death rate in 2011, which is approximately two, and the overdose death rate in 2015, which is approximately six per 100,000.

Q. And when you say "approximately", did you have the exact data?

A. Yes. I looked at the underlying data that comprised this figure, but you can see it pretty clearly goes from 2 to 6.

Q. And so, you used for this purpose the opioid-related

overdose deaths?

A. Illicit opioid overdose deaths.

Q. And the point you were making in making the fentanyl adjustment was that the mortality rate you had from Larney didn't actually capture the fentanyl phenomenon after 2011, right, that there had been this increase in fentanyl deaths and you needed to account for that in the mortality rate?

A. I was concerned that the mortality rate in Larney, as applied to today's epidemic, was too conservative because we know that people who use fentanyl have a higher risk of overdose given the relationship between dose and duration and overdose death.

Q. So, and what you did then for 2011, you took a baseline level of synthetic overdose deaths and then you looked at the change between 2011 and 2015; is that what you did?

A. Yes. It's called an interrupted time series method.

Q. So, let me point you back now to DEF-WV Exhibit 2587. And if you look at the last page of this document, it shows -- in the right-hand column it shows synthetic opioids other than Methadone. It shows deaths per 100,000 for synthetic opioids other than Methadone.

Do you see that?

A. I'm sorry. I -- so, this is --

Q. Defendant's exhibit 2587.

A. 2587.

Q. It's the -- the appendix?

A. Page 4?

Q. Yes.

A. Age-adjusted drug overdose death rates involving stimulants, by type of stimulant?

Q. No. I'm on the -- I'm on the Page 4 -- I'm sorry -- Page 3. Age-adjusted drug overdose death rates involving opioids, by type of opioid.

Do you see that?

A. I do.

Q. Are these the same data that you used?

A. No.

Q. They show -- they show deaths per 100,000 in the right-hand column. Would that be deaths per 100,000 for synthetic opioids; namely, fentanyl?

A. This data table has age-adjusted drug overdose death rates involving opioid separated out by the type of opioid.

Q. Right.

A. I didn't rely on this to come up with the estimate that I used in the OUD estimate. I used this estimation of illicit opioid overdose deaths. And I can tell you why. It's an important point.

Q. Why don't you explain why you did illicit overdose?

A. Because the estimate that we're trying to get to is the probability that you die of an overdose given that you've

used an opioid that contains fentanyl. So, you wouldn't want to use for that just the synthetic -- the total synthetic opioid death rate because what you want is the probability of a death given that you've used an opioid that contains fentanyl. So, those would be two different numbers.

And the illicit opioid overdose death rate is a closer approximation of the probability that you die given that you're using an opioid than the total number of T40.4 deaths per 100,000. That would not be the right -- that would not be the right quantity for the probability of death given that you've used an opioid.

Because that's what Larney is estimating, right? Larney is taking the total OUD population and estimating the probability of death. And so, I need the total OUD population and the probability of death if there's a fentanyl in the opioid; not what the synthetic opioid overdose death rate is, but the probability of death given that you've used an opioid.

And that's why it's, in my opinion, more appropriate to use the illicit opioid overdose death rate than just this simple T40.4 synthetic opioid death rate.

Q. So -- so here, if we go back to the Dowell paper and the Dowell paper shows roughly -- that in 2011 the illicit opioid overdose deaths are roughly two -- is that what you

say?

A. About two per hundred thousand.

Q. You don't know it exactly?

A. Not off the top of my head.

Q. Do you have a way to find it?

A. With a computer, I can.

Q. What is the way you would find it?

A. You could -- I mean, they use the CDC data. So, you could look up the CDC data.

Q. So, the Dowell data -- the Dowell paper is based on the CDC data?

A. This -- this estimate is. They also have prescription opioid sales and other -- the paper includes data other than the CDC WONDER data, but I -- this estimate is based on CDC WONDER data.

Q. And then -- and then you -- you ran that out to 2015, correct?

A. Yes.

Q. You ran out the increase in illicit opioid overdose deaths from 2011 to 2015, correct?

A. That's right.

Q. And so -- and, again, you don't know the precise number for 2015, correct? You're looking at this chart. You don't know the precise --

A. Right now, I'm looking at the chart, yeah. I don't --

I don't have that information stored in my working memory.
Q. And this Dowell paper is the only source you've cited for the data to make this adjustment?
A. I cited the underlying CDC data that I verified the numbers in Dowell with.
Q. And we could find in your work papers the precise numbers?
A. I'm sure you could. I'm sure it's in the spreadsheets that I sent.
MR. HESTER: So, may I have a moment to consult, Your Honor?
THE COURT: Yes.
(Pause)
BY MR. HESTER:
Q. Dr. Keyes, I just want to run through the numbers that you worked up to make sure we've got it all correct. So, your approach, the approach you followed, was you multiplied the Larney rate times 3, correct?
A. That's right.
Q. And that was based on your eyeballing that the Dowell data showed about 3?
A. It's based on the Dowell data, which is based on the CDC data.
Q. Now, in your report, you use the word "approximately". You said it was "approximately a change of 3." Was it

exactly a change of 3 or approximately?
A. I would have to go and look at the -- the numbers again.
Q. What's the reason that you used the word "approximately" in your report?
A. I think I was just trying to provide a general overview of my method.
Q. So, let me ask you just to confirm the numbers. So, your approach was to multiply Larney times 3 for the fentanyl adjustment, right?
A. That's right.
Q. And I think -- can you do the math for me, Dr. Keyes, just to confirm? If we multiply Larney times 3, and then we -- it would have to be Larney times 3 x .84.
A. Can I have a pen and scrap paper?
Q. Yes. Do you need some paper, too?
A. Yes, please.
Q. Okay.
A. So, we have 3 x 0.0052 and then we're multiplying that by .84, right?
Q. Yes.
A. Okay. I get 0.013104.
Q. And then you're able to recreate the number, the final OUD number that you came up with from that, correct?
A. I -- do you want me to --

Q. Yes. Could you do the final math? So, in other words, let's just be clear for the record. You multiplied Larney times 3, so it's .0052 x .84. That becomes your fentanyl mortality rate, right? Correct? And it's a weighted fentanyl mortality rate?

A. That's correct.

Q. And then you add that together with the non-fentanyl mortality rate?

A. That's right.

Q. And is -- are you able to recreate the exact number that you came up with for your OUD estimate?

A. I am doing it right now. You've given me a calculator and pen and math to do. This is like the best day.

Q. What could be better than this?

A. Okay. Yes. I've recreated the number.

Q. And the number is?

A. 8252.

Q. And that's -- that's the way you calculated the OUD population for Huntington-Cabell, right?

A. That's right.

Q. Now, I asked you before about your point, your use of the word "approximately". If -- if the approximation is not exactly 3, but if the number -- if the multiplier here were larger than 3 -- so, for instance, if the multiplier were a larger number and I'm going to -- I'm going to do an example

just to work it through with you, okay?

And I'm just putting up here, just so we don't get confused, 2015 unrounded. You ran this out to 2015. So, you were looking at the change -- when you came up with your three-times multiplier, you were looking at the change between 2011 and 2015, correct?

A. Yes. I don't -- sorry. I'm not understanding what "unrounded" means there.

Q. Well, I'll explain that.

A. Okay.

Q. I know that's my word and not yours.

A. Okay.

Q. So, let the record be clear that's my word I wrote out just to help me and we can change it to something else.

A. Okay.

Q. But you used the word "approximately" and I just want to ask you to work through a number with me and it's really to assume something. It's not to say that it's right, but it's to assume.

And I want you to assume that the approximate number is actually rounded and that the real number is 3.875. And if you assumed that, Dr. Keyes, if you assume that the real number --

MR. HESTER: May I consult with my colleague for a minute?

THE COURT: Yes.

(Pause)

BY MR. HESTER:

Q. I'm going to actually change my assumption, Dr. Keyes. I want you to assume with me that the proper number is 3.27 times Larney. I want you to assume that. Can you run the math for me on what that would be?

A. Sure. Looks like about 8,051, if I'm doing my math right.

Q. I'm not sure that you are, Dr. Keyes.

A. Oh, no. I can try it again. Okay.

Q. So, you multiply --

A. So 0.0052 x 3.27, right?

Q. Yeah. I mean .0327.

A. .0327? We're multiplying --

Q. Oh, sorry. You're right.

A. Okay.

Q. Sorry. So, it would be 3.27 x this .0052?

A. So, that's .017004 --

COURT REPORTER: I'm sorry. Can you repeat that number one more time?

THE WITNESS: Yes. .017004.

COURT REPORTER: Thank you.

THE WITNESS: And we're multiplying that number then times .84, correct?

BY MR. HESTER:

Q. Yes, to create your fentanyl adjustment.

A. Yeah. So then, I get 0.01428336.

Q. .01428?

A. Yes.

Q. Yes.

A. Is that right.

Q. Yes. And so, that adds up to .01511 that you divide into 115; is that right?

A. Well, let's just see. Then we've got 0052 x .16, which is 0.000832.

Q. You've already got that one, yeah.

A. Right. Sorry. I'm just -- and then we're adding. So, our denominator is 0.01511536; is that correct?

Q. Right. And you divide that into 115, correct?

A. Okay, got it. 7608.

Q. Now, let me ask you to make another assumption with me. You ran -- you ran your numbers out to 2015 for making this fentanyl adjustment, right? You looked at the period between 2011 and 2015 and that was the period that you looked at.

If you ran the fentanyl numbers out to 2018; in other words, if you looked at the change in synthetic overdose deaths over the whole -- over the period up to 2018, it would also have it -- it would change the OUD numbers,

correct?

A. That wouldn't be the right methodology to use.

Q. I didn't ask you that.

A. Okay.

Q. I asked you if you did it, if you ran the --

A. I did not do that.

Q. And so, let me -- let me try to do that one. So, in other words, you're measuring OUD numbers for 2018, correct?

A. That's right.

Q. You're trying to come up with an OUD population that applies to 2018?

A. Yes.

Q. And so, if you looked at the change in synthetic overdose deaths from 2011 to 2018 --

A. But I'm sorry. I don't understand why you would do that.

Q. Well, I'm asking the "if". I'm asking you to assume with me. I want to understand the sensitivity of the numbers. The --

MR. FARRELL: Objection, Your Honor. The witness has testified this is not proper methodology. So, as long as the record is clear that she's using some methodology proposed by Mr. Hester, but this is not a methodology that she has adopted or is endorsing.

THE COURT: Well, you're using this to question

the methodology she did use, aren't you?

MR. HESTER: That's what I'm trying to do, Your Honor. It's an assumption to test the methodology.

THE COURT: Mr. Farrell.

MR. FARRELL: I believe the witness just testified that she would not use this for this purpose and attempted to explain.

THE COURT: Well, I think it's proper cross examination and I'll allow it. Go ahead.

MR. FARRELL: Can I also ask for a foundation to where 3.27 comes from rather than just theoretical or fictional?

MR. HESTER: Well, Your Honor, I don't think I'm obliged to, but I think I will be able to set the foundation for it. I -- I can do that, but I -- I would like to work through the numbers first.

THE COURT: Go ahead.

BY MR. HESTER:

Q. If we -- if we looked at the period from 2011 to 2018 to derive your fentanyl adjustment and, during that period, I want you to assume with me that the change reflected in the CDC data is 6.36 --

A. Is that using the same definition that Dowell used --

Q. Yes.

A. -- in this, the illicit opioid overdose deaths?

Q. Yes. Now -- yes. And I'm going to set the foundation with you, but I want you first to assume -- you know -- first of all, you know that fentanyl deaths have continued to rise after 2015.

A. Yes. That's why we have the weighting procedure.

Q. Right. And so, what we see from 2011 to 2015 is some increase in fentanyl deaths.

A. The start of the increase, which is very important for the methodology.

Q. Well, okay.

A. Okay.

Q. And, in fact, the death rates increase, continue to increase into 2018, correct?

A. The death rate did, but the probability of death given use did not.

Q. Well, if there's more fentanyl being mixed into the heroin supply and being mixed into the drug supply from 2018 as compared to 2017, or 2016, or 2015, that increases the likelihood of death from fentanyl, correct?

A. No. That's the key to the methodology that I think I would like to explain.

Q. Well, let me -- let me keep going on this.

MR. FARRELL: Objection, Your Honor. Can she explain?

MR. HESTER: So, no. I don't think she's

answering my question.

MR. FARRELL: I'm sorry, Judge?

THE COURT: I'm going to let him continue and finish and we'll see where we go. And she can be re-directed on this, if you want to.

BY MR. HESTER:

Q. So, let me assume -- let me ask you to assume that if you looked at the period 2011 to 2018 the change in the numbers is not 3 times, but the change is 6.36.

A. But that's not what that number represents.

Q. I'm asking you to assume it, Dr. Keyes.

A. Right, but your -- it's based on assumptions that are not what that number is representing.

Q. Dr. Keyes, you measured this approximately three times by looking at this Dowell chart and seeing that there had been a change in overdose deaths during the period from 2011 to 2015, right?

A. During the start of the increase of the fentanyl period, which is why it is an appropriate methodology for the parameter I'm trying to estimate, but going to 2018 would not be appropriate.

Q. I'm not asking you whether it's appropriate right now.

A. Okay.

Q. I'm asking you to test the assumption. And the way you did this, just going back to Dowell, Exhibit 2497, is you

looked at the change between 2011 and 2015 in illicit opioid overdose deaths, right?

A. Yes. It's a procedure called an interrupted time series analysis.

Q. And you looked at the change between 2011 and 2015 to figure out your three times adjustment?

A. That's right.

Q. If you looked at the change between 2011 and 2018, there would be a larger change in illicit opioid deaths, correct?

A. There would be a larger change, but it would not be a correct change to use for that number. This is -- that's why I didn't do it. I did this in 2018. I could have used the 2018 numbers.

Q. Well, it would have shown your OUD number, right?

A. It would not have been an appropriate methodology to use. It shrinks the OUD number anyway because I weight it based on the proportion of cases that are T40.4.

So, if I used a bigger number for the multiplier, then I wouldn't have weighted for the proportion of deaths that are T40.4. The proper methodology that shrinks the OUD number is to use the interruption of the time series given the introduction of fentanyl and then weight that probability by the probability of deaths that are T40.4.

Q. But you looked over a four-year period to figure that

out, to figure out your three-times multiplier? You looked over a four -- year period?

A. That's right.

Q. I'm just asking you to work with me. Instead of looking over a four-year period, I want you to look over a seven-year period.

A. Okay.

Q. And if you look over a seven-year period and if you assume that the change is 6.36 --

A. Okay.

Q. I want you to do that math for me.

A. However, I just have to say, if you do that, then you shouldn't use the weights that I also provided. We should just do 6.36 x 0.0052 and divide the 115 by that. It would not be appropriate to do both of those things.

Q. This weighting that you used, this weighting that you used, the 84 percent weighting for fentanyl was based on the breakdown of deaths during 2018, correct?

A. That's right.

Q. Okay. Let's go back. I want you to assume that the proper multiplier is 6.36 x Larney. Are you able to do that math for me?

A. 0.0052 x 6.36 is 0.033072.

Q. And then, what is the -- say that again, Dr. Keyes.

A. 0.033072.

Q. And then what is the OUD number that you estimate?
A. Should -- do you want me to include the weighting or not include the weighting?
Q. Yes. I'm asking you to use the --
A. So, we're double weighting for --
Q. I'm asking you to use the same weighting you used based on the 2018 deaths and I'm just asking you to use that and is it -- can you tell me what the OUD number would be?
A. I get 3,391.9.
Q. 3,391; is that correct? That's what you calculated?
A. That's the calculation.
Q. Now, let me ask you to look back at the Dowell paper, please. No, I'm sorry, not the Dowell paper. I want you to look back at DEF exhibit WV 2587 and I want you to look at the data table for figure 3, which is on Page 3 of this document. Do you have that?
A. I do.
Q. And so, your point is that one should look at all illicit opioid overdose deaths to figure out the CDC data? In other words, we shouldn't just look at the synthetic opioid number? We should also look at other illicit opioids, correct?
A. Well, not exactly. The point is that the perimeter that we're trying to estimate is the probability of death given OUD and that the interruption of the time series

between 2011 and 2015 for illicit opioid deaths provides the best approximation of that.

Q. So -- so, in your -- if you look back at the Dowell paper, that's the one you said you used, correct?

A. That's right.

Q. And the Dowell paper has this line in the graph for illicit opioid overdose deaths, correct?

A. Correct.

Q. And so, I'm trying to get to the precise data instead of looking at this graph. And so, for that purpose, I want to point you to DEF Exhibit 2587, Page 3.

A. This does not have the data that underlie that graph. These are separated by each T code separately, but this combines several T codes. So, we can't -- we can't compare them directly. We can't get the exact number from Figure 3.

Q. I'm going to ask you to work with me again. If I look at this exhibit, the data table for Figure 3, there's a -- there's a column for deaths per 100,000 for heroin, right?

A. Yes.

Q. And there's a column for synthetic opioid deaths other than methadone, correct?

A. Yes.

Q. And so, if we add those two together, that's a measure of illicit opioid deaths, right?

A. No. You can't add them together because they're not

mutually exclusive. As we previously talked about, there can be multiple T codes listed on a death certificate.

Q. So, you could have circumstances where you have multiple -- multiple causes of death listed in these death certificates in there, so you can't add them together; is that what you're saying?

A. That's what I'm saying.

Q. If you -- whether you agree with these specific numbers or not, Dr. Keyes, the broader point here is that if the mortality rate is too low, if the estimated mortality rate is too low, your estimated OUD population is going to be too high, correct?

A. That's right.

Q. And so, for instance, if your fentanyl adjustment is too low, if this is lower than it should be, you're going to be overestimating the OUD population?

A. This is why we do corroboration analyses and talk to people in the county to try to corroborate.

Q. But can you answer my question first? If your fentanyl adjustment is too low, then you're going to be overestimating the OUD population, correct?

A. It's possible.

Q. Well, that's what would happen if your fentanyl adjustment is too low.

A. The OUD estimate is a function of the underlying

denominator data. So, if the denominator changes, the OUD estimate will change.

And so, if you use a different multiplier for fentanyl, if your multiplier goes up, then the OUD population would go down.

Q. But, in particular, if the fentanyl adjustment that you've picked is lower than it should be, lower than what the reality is, then you're going to overestimate the OUD population under this formula?

A. Yes.

Q. That was fun. So, let's put that aside for a minute, Dr. Keyes.

A. I'm happy to bring out the calculator anytime you have another mathematical question.

MR. ACKERMAN: Mr. Hester -- or can we save whatever's on that screen?

MR. HESTER: Yes. Yes.

MR. ACKERMAN: I just want to make sure we get it.

MR. HESTER: I want to make sure I press the right buttons to save it.

MR. ACKERMAN: Before it disappears, exactly.

MR. HESTER: Confirm, right?

BY MR. HESTER:

Q. So, Dr. Keyes, putting aside this discussion that we've just been having about the fentanyl adjustment and the

Larney data, I want to go back to your OUD estimate and, as we discussed, the number that you estimate is 8,252 people with OUD in Huntington-Cabell, correct?

A. That's right.

Q. And that's reflected, for instance, in your August 24 errata that I've given you, correct, at Figure 14?

A. Yes.

Q. So -- so, you have a total number of 8,252 individuals with OUD that you estimate for Cabell-Huntington, correct?

A. That's right.

Q. And of that number, you allocate 5,800 of those OUD cases directly to prescription opioids; you directly attribute them, correct?

A. I do.

Q. And that applies your attribution methodology that we discussed earlier?

A. That's right.

Q. And so, that means approximately 70 percent of the OUD cases in your analysis are directly attributable to prescription opioids?

A. I haven't done that math, but I trust that you have.

Q. I have. It's 5,800 divided by 8,252. It comes out to about 70.82 percent. Sound about right?

A. That sounds about right.

Q. And then, you also estimate that 1,309 of the OUD cases

are indirectly attributable to prescription opioids, correct?

A. That's right.

Q. So, that's approximately 16 percent of the OUD cases that are indirectly attributable to prescription opioids and that would be 1,309 divide by 8,252?

A. Yes.

Q. And, again, when you do this indirect attribution, you're doing that based on the methodology we discussed earlier today, correct?

A. Correct.

Q. And so, if you add up those OUD cases, the ones that you directly attribute to prescription opioids and the ones you indirectly attribute, the total is 7,109 OUD cases, correct?

A. Yes.

Q. And that's 5,800 added to 1,309, correct?

A. Yes.

Q. So, out of the 8,252 OUD cases -- or OUD people or -- I'm sorry. Maybe I'll back up.

Out of that total number that you've estimated of 8,252 people with OUD, you attribute 7,109 to prescription opioids either directly or indirectly, correct?

A. That's right.

Q. That means 1,143 OUD cases are not attributable to

prescription opioids in your methodology either directly or indirectly, correct?

A. Correct.

Q. And that represents just about 14 percent of all the OUD cases in Cabell-Huntington that you've estimated, correct?

A. That's right.

Q. Dr. Keyes, I'd like to switch gears a bit to discuss trends relating to prescription opioids. At Page 15 of your report, and I think you have it there, you state that the opioid prescribing rate in Cabell-Huntington -- no, in Cabell County, sorry, was 186.6 prescriptions per 100 persons in 2011; is that right? Do you see it there on Page 15?

A. 186.6 prescriptions per 100 persons from 2006 to 2011. So, yes.

Q. Right. So, I've got that right? The number you came up with for 2011 for the prescribing rate in Cabell County was 186.6 prescriptions per 100 persons?

A. That's right.

Q. And then, on the same page, you state that the opioid prescribing rate declined at 92.1 prescriptions per 100 persons by 2018, correct?

A. That was the most recent year-end data available then. There's since been 2019 data that has been released.

Q. And I'm really focusing on these numbers in your report. You're showing more than a 50 percent decrease in the level of prescriptions in Cabell County, prescription opioids in Cabell County from 2011 to 2018, correct?

A. That's from the highest point to the lowest point, but it's not from the pre-opioid epidemic point.

Q. Let me ask again.

A. Sorry.

Q. Between 2011 and 2018, you're showing more than a 50 percent decrease in the level of prescribing of prescription opioids in Cabell County, correct?

A. Yes.

Q. And you're also aware that there's been a decline in MME per person of prescription opioids in West Virginia statewide, correct?

A. Yes.

Q. And in your report you state that the MME per person in West Virginia decreased 2.4 percent from 2010 to 2015, correct? That's at Page 15.

A. Yes. The decrease was slower than the U. S. average, but it was 2.4 percent.

Q. So, the 2.4 percent decrease in the MME per person in West Virginia from 2010 to 2015?

A. Yes.

Q. And then, from 2016 to 2017, the MME per person in West

Virginia decreased by 15.1 percent, correct?

A. That's right.

Q. You previously testified, Dr. Keyes, that the non-medical use of prescription opioids means using them in a way other than is prescribed by a doctor, correct?

A. Yes.

Q. And the non-medical use of prescription opioids is declining in West Virginia, correct?

A. I believe it is.

Q. And in 2015 to 2016, I can point you to your report at Page 40. In 2015 to 2016, 1.2 percent of non-institutionalized West Virginians used opioids non-medically in the prior month?

A. Well, I have to qualify that. That's based on the National Household Survey of Drug Use and Health Data and there's now -- that's an underestimate, we know, of non-medical use and, in fact, there are some papers that have recently come out suggesting that, nationally, we're seeing increases in OUD; whereas, NSDUH is showing slight declines. So, I would say that the NSDUH data shows that the prevalence of non-medical use is slightly declining, but we know that to be an underestimate.

Q. Well, let me ask you, your report states that available evidence indicates that non-medical pain reliever use, primarily opioids, is declining among non-institutionalized

mostly household populations in West Virginia overall from 1.2 percent of those in West Virginia in the sampling framed reporting past month use which --

A. Right, but that section also qualifies --

COURT REPORTER: I'm sorry. Can you -- you were overlapping. I'm sorry. Do you want to finish your question so I can --

BY MR. HESTER:

Q. Yeah. I hadn't finished. Sorry. So, there was decline, you state in your report, a decline in non-medical pain reliever use among non-institutionalized mostly household populations from 1.2 percent of those in West Virginia in the sampling frame reporting past month use in 2015 to 2016 to .90 percent in 2017 to 2018, correct?

A. Yes.

Q. And your report also says that by 2017 to 2018, that percentage had declined by 25 percent to 0.9 percent, correct?

A. Can you -- which page of the report?

Q. Sorry. Page 40. So, I'm really just --

A. So, I say that the non-medical use of prescription --

COURT REPORTER: I'm sorry. Can you slow down for me, please?

THE WITNESS: I'm sorry.

It says non-medical use of prescription pain relievers

has been relatively stable in recent years from 2.86 to 2.89 in 2016-2017 and 2017-2018 respectively. And reports of heroin use in the past year among adolescents in West Virginia from .7 to .9 percent in 2016-2017 and 2017-2018.

Q. I think you're focusing on a section dealing with adolescents. I wanted to point you to the statement up above in your report.

A. Oh, I see. So, we're focusing just on adults?

Q. Yes. So -- so, the prior paragraph in your report at Page 40 is talking about adult non-medical use of pain relievers; primarily opioids, correct?

A. Yes.

Q. And it states that the non-medical use of non-pain -- non -- sorry. Let me start over.

It states that the non-medical use of pain relievers; primarily opioids, is declining among non-institutionalized mostly household populations in West Virginia overall from 1.2 percent of those in West Virginia in 2015-16 to .9 percent in 20170-2018.

Do you see that?

A. I see that.

Q. And that's a correct statement of the data?

A. Well, not exactly because, as the next sentence documents, Drug Use Disorder is increasing. So --

Q. I wanted to -- did you correctly state the data that I

read?

A. That sentence is -- you read the sentence correctly, but it goes with the next sentence about Opioid Use Disorder, which is what we're focused on.

Q. And the Opioid Use Disorder that you're describing in the next sentence would include -- would include heroin and fentanyl use, correct?

A. That's right.

Q. Let me ask you to look at another document, please.

MR. HESTER: May I approach, Your Honor?

THE COURT: Yes.

BY MR. HESTER:

Q. Dr. Keyes, we've handed you a document marked as MC-WV 01864, which are the NSDUH 2017 state tables. Do you have that in front of you?

A. I do.

Q. And this report contains statewide data from the National Survey on Drug Use and Health, correct?

A. That's right.

Q. And you considered this report in forming your opinions in this case?

A. I did consider it.

MR. HESTER: And let me ask Your Honor to move this into evidence as a public record.

THE COURT: Any objection?

MR. FARRELL: Your Honor, I'm not quite sure what the foundation of it is for other than the representation of Mr. Hester --

MR. HESTER: Well, I believe Dr. Keyes said she relied on it.

THE COURT: Well, if it's a public record --

MR. FARRELL: I'm not sure what it is.

BY MR. HESTER:

Q. Dr. Keyes, you're familiar with the National Survey on Drug Use and Health, correct?

A. I am.

Q. And you reviewed data from NSDUH in your work, correct?

A. I did.

Q. And, in fact, you considered this report in your materials? It's Reference 589 of your report, if you want to look at it.

A. I considered many materials.

Q. This is one you would consider?

A. And this is -- this is one of hundreds.

MR. HESTER: Should I proceed, Your Honor, or do you -- should I wait?

THE COURT: Well, have you laid the basis for it under 803(8), Mr. Hester?

MR. HESTER: I -- I believe I've laid the basis, Your Honor, that she's familiar with it. This is a document

she relied on. She's familiar with this data for purposes of her work and I believe it's a public record published by the U. S. Government.

THE COURT: Do you object to it, Mr. Farrell?

MR. FARRELL: Yes, Your Honor. Reliance by an expert is not a basis alone for admission.

THE COURT: Well, I think that's right and I don't think you've hit all the points you need to hit to get it in under 803(8), Mr. Hester, so I'm going to sustain the objection at this point and let you go ahead with your questions.

MR. HESTER: All right. Thank you, Your Honor.

BY MR. HESTER:

Q. Dr. Keyes, if you look at Page 42 of this document, Table 21 has data on Pain Reliever Use Disorder in the past year by age group and state, correct?

A. That's right.

Q. And in West Virginia it shows the percentage of adults over the age of 18 with Opioid Use Disorder in 2015 and 2016 was 0.91 percent, correct?

A. This is on the next page, right, 43?

Q. Yes. I think so, yes.

A. And, I'm sorry, what column are you referring to?

Q. It shows -- I was looking at the column over on the right-hand side for people 18 and over in 2015 to 2016. It

shows a percentage of people with OUD in West Virginia of .91 percent; is that correct?

A. No. This is a household sample. So, it excludes anyone who is at high risk for Opioid Use Disorder. So, in a low risk population, the prevalence as estimated by NSDUH is .091.

Q. So, you're saying it doesn't include people who are incarcerated or homeless?

A. For example.

Q. But it does include people who live in households?

A. It includes a sample of people.

Q. And let me ask you then to look at the NSDUH Report from 2019.

A. Well, before we move on, we should note that the decrease between 2015 to 2016 and 2016 to 2016 [sic] was not statistically significant. So, I don't think it would be accurate to say that it decreased.

Q. I haven't finished yet. So, I have one more I wanted to show you.

MR. HESTER: Your Honor, may I approach?

THE COURT: Yes.

Q. Dr. Keyes, I've handed you Exhibit MC-WV 1866, which is the NSDUH 2019 state data tables.

Do you see that?

A. Yes.

Q. And do you recognize this is a newer version of that same report that NSDUH puts out annually?

A. I do.

Q. And the point you were making previously that NSDUH is not comprehensive doesn't necessarily mean that comparisons between years are not valid, correct?

A. Unfortunately, in the case of the NSDUH, it does, and I believe across these years there was a change in the way they asked the questions about prescription pain reliever use. And so, they have explicitly stated on their website that you cannot compare years.

Q. So -- so, you -- you believe you can't compare years between NSDUH data?

A. Well, not all years, and it really depends on the measure that you're looking at it depends on what year you're trying to compare to what year. So, you just have to be careful with the data because they change the questions sometimes and they make those comparisons. Sometimes, you can't compare them.

Q. What year did they change the data?

A. I don't -- off the top of my head -- I would have to go to the NSDUH and website and look. I assume that it's stated on there.

Q. Let me just ask you just one quick question on this and then we'll move along. If you look at Page 44 of this

document, it states that the percentage of West Virginians over the age of 18 with Opioid Use Disorder was .63 percent.

Do you see that?

A. Page 44?

Q. Yes.

A. That's Alcohol Use Disorder.

Q. Let me take you over to --

A. Or 43?

Q. 43. Sorry. Do you see the number for the column for 2018-2019? People 18 and over, the percentage with Opioid Use Disorder listed as .63 percent?

A. The proportion of people in the NSDUH sample, yes.

Q. So, as between these two years, if you look at these two documents together, and taking account of your point, I'm just asking you the question, if you looked at these two data sources together, it would show a decline in Opioid Use Disorder of -- from .91 percent in 2015-2016 to .63 percent in 2018-2019?

A. No. Unfortunately, you can't draw that conclusion from these reports. What those reports show is -- the first report shows no statistically significant decrease and the second report shows no statistically significant decrease. The P value is .178.

And you can't compare between the two reports. Even if the methodology didn't change, they're not doing a

statistical test across those years.

So, as an epidemiologist, my conclusion would be you've got two reports that both show there's been no change.

Q. Well, but it can't be quite right, Dr. Keyes, because the P value here is only between two years. It's between 2018-2019 and 2017-2018, right? That's the way they measure the P value?

A. Right, but there's no P value for 2015 to 2019.

Q. It hasn't been provided?

A. Right. You've got two non-significant P values.

Q. Your --

A. So, the only conclusion that you can draw here is you've got two reports of four years and, in the first two years, there's no change and, in the second two years, there's no changes.

Q. But let me just make clear one point. The P values that are reflected, for instance, in this document we're looking at right now, which is Exhibit 1866, and we're at Page -- I guess 43 of this document, those -- the P values shown there is comparison between the two years of data that are shown. It's between 2017-2018 and 2018-2019, right?

A. That's right.

Q. It doesn't provide a P value for the data between 2015 and 2018?

A. Which is why it would be inappropriate to conclude that

there would be a change over time documented here.
Q. The P value could be computed, correct, for that longer period?
A. You'd have to look and see whether that would be appropriate based on the NSDUH data if there had been a change in measurement.
Q. If there hasn't been a change in measurement, you could look at the P value between a longer period of time that's just not provided here, correct?
A. Yeah. One could do that. And, theoretically, one can look at changes over a longer period of time.
Q. Next, I'd like to talk a little bit more about --
THE COURT: It may be time for a break, Mr. Hester.
MR. HESTER: Yes. That's a good time, Your Honor, a very good time.
THE COURT: Okay. Let's take about ten minutes.
(Recess taken)
(Proceedings resumed at 3:42 p.m. as follows:)
THE COURT: Okay.
MR. HESTER: Thank you, Your Honor. May I approach?
THE COURT: Yes.
BY MR. HESTER:
Q. Dr. Keyes, I've handed you a document marked

Defendants' West Virginia 2647. It's entitled "Associations of Non-Medical Pain Reliever Use and Initiation of Heroin Use in the United States."

Dr. Keyes, have you seen this document before?

A. Yes.

Q. And I take it this is a document you rely on in your report; correct?

A. It is.

Q. And under the heading of Author Affiliation it says that Pradip K. Muhuri and Joseph C. Gfroerer are with the Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services, Rockville, Maryland.

Is that your understanding as to the author affiliations?

A. I don't see here their affiliations.

Q. If you'd look at Page 16.

A. Oh.

Q. I'm sorry. I should have pointed you to this page, Dr. Keyes.

A. I see.

Q. So it states that Pradip Muhuri and Joseph Gfroerer are with the Substance Abuse and Mental Health Services Administration of the Department of Health and Human Services. Do you see that?

A. I do.
Q. Is that consistent with your understanding?
A. I don't know them and I, I -- but I have no reason to believe otherwise. I believe -- I'm sure -- I would assume -- I have no reason to know that what is stated here is not the case.
Q. And as the title of this article suggests, the article looked at the relationship between non-medical opioid use and heroin initiation; is that right?
A. Yes. They measured non-medical -- the, the NSDUH data that we've been talking about only measures non-medical data.
Q. So this paper was looking at the association between non-medical use of prescription opioids and heroin use; correct?
A. That's right.
Q. It wasn't looking at the relationship between medical use of prescription opioids and heroin use?
A. Well, that's, that's -- it actually is because of the overlap in those two groups. We know that most non-medical users also obtain prescriptions medically.
Q. Yes. But, but the point here is that somebody might obtain some prescription opioids medically, but they are viewed as non-medical users for purposes of this study; correct?

A. They at least used opioids once non-medically as far as I think that we could say based on what is assessed in the study. But most non-medical users have also used medically.

Q. Let's be clear on the terminology here. When, when you speak about a non-medical user, they might have had a prescription or they might have a prescription, but the focus of a study like this is on people who are using prescription opioids non-medically; correct?

A. They are at least using non-medically. They may also be using medically. And, in fact, because those two populations overlap, we can -- they're not only using non-medically I guess is what I'm saying.

Q. They might be using some opioids medically, but they're also using opioids, prescription opioids non-medically; correct?

A. That's right.

Q. And they're not included in the survey unless they are engaged in at least some non-medical use of prescription opioids; correct?

A. Exactly.

Q. And, so, -- and it's reflected in the title of the document. They're looking at the relationship or the association between non-medical use of prescription opioids and heroin use; correct?

A. That's right.

Q. If you look at -- if you look at Page 1 of this document in the abstract in the left-hand column, there's a -- there's two statements.

One statement is, "Four out of five recent heroin initiates previously used non-medical prescription --"

Actually, I should back up to make it clear we're on the same language.

Do you see the references throughout this paper to NMPR?

A. Yes.

Q. And that means non-medical prescription pain relief, reliever use; correct?

A. That's right.

Q. And, so, that's what they're talking about here when they say NMPR; right?

A. That's right.

Q. So it states in the, in the abstract, "Four out of five recent heroin initiates previously used NMPR."

Do you see that?

A. I do.

Q. And is that the statistic that you cited in your prior testimony?

A. There are many studies that show a similar estimate. This is one of them.

Q. And then it goes on to say, "However, the vast majority

of NMPR users have not progressed to heroin use."

Do you see that?

A. I do.

Q. And does that accord with your understanding that the vast majority of people who use prescription opioids non-medically do not progress to heroin use?

A. Yes.

Q. And then it goes on to say only 3.6 percent of non-medical prescription users had initiated heroin use within a five-year period following their first non-medical prescription opioid use. Do you see that?

A. I see that's what is written.

Q. And, and does that accord with your understanding?

A. I mean, 3.6 percent initiating heroin use is a -- quite a large transition probability. So I guess I would only -- I would take issue with the word "only." 3.6 percent is a lot of heroin.

Q. I don't think that answered my question. My question was: Does it accord with your understanding that only 3.6 percent of people who are using prescription opioids non-medically initiated heroin use within the five-year period following their first non-medical use of prescription opioids?

A. I believe that's what this study found if that's the question.

Q. And, so, that means that putting it the other way around, 96.4 percent of the non-medical prescription pain reliever users did not use heroin within five years of their first initiation of non-medical use of prescription opioids?

A. That's right.

Q. So I'm going to start a new board.

We have this one saved; correct?

So, Dr. Keyes, I've written on the board here "gateway." And the first thing I wanted to do was put up the number that we just discussed which was that 96.4 percent of non-medical users do not transition within five years of first non-medical use. I want to just put that up as a reference so we don't lose it.

A. In the household sample if you would add that, please.

Q. And that, that 96.4 percent, as we just discussed, reflects the finding of this Muhuri article; correct?

A. That's right.

Q. And you make the same observation in your own report at Pages 47 to 48 of your report if you want to look at your report. You state that the absolute risk of transitioning to heroin, given prescription opioid use, is relatively small. Do you see that?

A. What page?

Q. 47 to 48 of your report.

A. I say a small but significant proportion of individuals

who use prescription opioids progress to heroin use.

Q. I was looking for the one -- I guess it's actually at the top of, top of Page 48.

You say, "The absolute risk of transitioning into heroin, given prescription opioid use, is relatively small."

Do you see that?

A. Well, could we read the whole sentence just for context?

Q. No. I wanted to focus on that clause first. And I wanted to focus on the fact that you state, "The absolute risk of transitioning to heroin, given prescription opioid use, is relatively small."

Do you see that?

A. I think out of context it's not really interpretable because you have to look at the whole sentence which includes the risk ratio estimate and the public health burden. So out of context, one clause is not really interpretable.

Q. Well, I wanted to ask you the basis for your statement, "The absolute risk of transitioning to heroin, given prescription opioid use, is relatively small."

What's the basis for that statement?

A. I think the studies that I cite in the report are the basis.

Q. And Muhuri would be one of those that you rely on for

that purpose?

A. Muhuri is one of several studies.

Q. Let me put that on the board. I wrote "absolute risk of transition small" to reflect that statement from your report, Dr. Keyes.

A. The first part of the sentence is that the number of individuals who use prescription opioids is approximately seven times larger than the number who use heroin. So that's probably an important point on that too. The point is that while the absolute risk is small, the population prevalence is large.

Q. In other words, your point is prescription opioids are widely used as medicines in this country; correct?

A. That's right.

Q. And, in fact, the data we looked at previously today reflected that almost a third of adults in 2014 received a prescription for opioids; correct?

A. I believe you said 245 million.

Q. Actually, I may be low. So that could be more than -- it could be over 60 or 70 percent of the population of the country; right?

A. That's right.

Q. So, in other words, the point is there's a large volume of prescription opioids being prescribed by doctors in their judgment of medical needs; correct?

A. There's a large supply of opioids. That's certainly the case.

Q. Well, and that's being prescribed by doctors who are prescribing them to patients; correct?

A. Some of them are being prescribed by doctors, correct.

Q. Well, most of them are being prescribed by doctors; correct?

A. Yes, most of them are being prescribed by doctors.

Q. And so, and so your point is it's a large volume of opioids because a large percentage of the country is being treated with opioids?

A. Right. So if there's a small risk -- it's sort of like smoking and lung cancer which I think I cite in the, in the report.

The prevalence of lung cancer is much lower than the prevalence of heroin use. And there's a lot of smokers in the U.S. So most smokers don't develop lung cancer. And, in fact, many more people use prescription opioids and transition to heroin use than smoking and get lung cancer. So you can't really look at the absolute risk in a vacuum. You have to look at the prevalence as well.

Q. But the, but the point is if you have an extremely large percentage of our country that is using prescription opioids for medical purposes, there could be some percentage of people who develop OUD as a consequence; correct?

A. Right. So if you take the 245 million number, for example -- and I think you said that 65 percent are of short duration?

Q. Yes.

A. I mean, we could work that through. That, that would be 160 million people on short duration. And with an event rate of .12, that's 200,000 people a year developing OUD from short duration opioids.

Q. Or put it the other side, put it the other way around. It also suggests the fact that 245 million people receive prescriptions in a given year for opioids reflects a broad scale judgment by doctors about prescribing opioids to treat pain; correct?

A. There is a lot of opioid prescribing in the U.S. And, therefore, small risk translates to big population changes. And, so, yes, there is a vast over-supply of prescription opioids in the U.S. And the majority of those people will not have a problem related to opioids.

But when you have 200,000 people a year -- and that's just the 160 million who are prescribed for less than three weeks. We've got 85 million, based on what you cited earlier, that are prescribed for chronic conditions where the event rate is much higher. And that doesn't include non-medical use.

Q. But I'm asking, I'm asking the point the other way

around. I'm, I'm trying to confirm that when you see a very large volume of opioids being prescribed, it reflects a widespread judgment by the medical community about the appropriateness of those prescriptions.

A. I don't think it necessarily reflects a judgment about the appropriateness. I think it reflects a, a decision based on the information at hand, of which the information can change.

Q. Well, you, you testified previously that the decisions made by doctors are overwhelmingly in good faith. The prescribing decisions on -- related to opioids are overwhelmingly in good faith. Correct?

A. They're in good faith based on the information that's available.

Q. And so, and so when the doctors are acting in good faith to prescribe that volume of pills, it reflects a widespread judgment by doctors about the appropriateness of that prescribing behavior; correct?

A. I don't know that I would conflate those two statements.

Q. So let's talk a little bit about how someone actually transitions from prescription opioid use to heroin use.

First of all, all of the studies that you've cited in your report in support of your opinion regarding the connection between prescription opioids and heroin are

measuring an association between the misuse of prescription opioids and heroin use; correct?

A. The studies that I cite in the report include medical use followed by transition to heroin.

Q. That's not, that's not what I asked you. I asked you the question: All of the studies you've cited in support of your opinion regarding the connection between prescription opioids and heroin all measure an association between misuse of prescription opioids and heroin use; correct?

A. Incorrect.

Q. Let me ask you to look at your report, please, Page 37. I'm trying to make sure I've got the right quote for you, Dr. Keyes.

MR. HESTER: May I consult just a minute, Your Honor, with my colleague? I'm sorry.

(Pause)

BY MR. HESTER:

Q. Dr. Keyes, I'm trying to find a statement -- a page in your report. I'm going to read you a quote and see if this is accurate.

A. Do you have a page number?

Q. I'm trying to find it.

Let me read this to you, Dr. Keyes. I have this in my notes. I'm going to find the page for you, so I will find this page reference. But let me read this and see if this

sounds correct to you.

"I reviewed 16 studies that found that individuals who use prescription opioids non-medically have higher rates of injecting and snorting heroin than individuals who do not use prescription opioids even after controlling for health and mental health as well as demographics."

Is that correct?

A. Well, I think in the context in that paragraph, I also talk about the studies of medical users. Many of the individuals in those studies were medical users.

Q. Well, we've gone through this before. Somebody could be a medical user but they're engaged in non-medical use of opioids; correct?

A. That could be the case.

Q. So it's Page 46. And it states in the first paragraph under the heading I -- second paragraph there's a reference to the fact that you reviewed 16 studies that found that individuals who use prescription opioids non-medically.

All of the studies that you were looking at were non-medical?

A. No, that's not correct. There were many individuals in those 16 studies who used opioids medically.

Q. But all of the studies were looking at non-medical use of opioids?

A. Not necessarily. The studies varied in terms of the,

the populations that were examined. And, so, there are many examples in these studies of individuals who used medically.

Q. That's not the question I'm asking, Dr. Keyes. The question I'm asking is that all of the 16 studies that you relied on for your analysis of gateway were based on people who were using opioids non-medically. Whether they were also people who held a prescription or not, they were all non-medical users. They were all studying non-medical users.

A. That's not the case. I think if you go and look at the studies, there are several in which there's information about medical users.

Q. So where it states, "I reviewed 16 studies that found individuals who used prescription opioids non-medically." 16 studies looked at individuals who used opioids non-medically. That was the study set you looked at; correct?

A. If you look at the populations that comprised the studies, there were individuals who were using opioids non-medically, many people for whom, you know, their first prescription was based on back pain, et cetera. Some of them went on to use non-medically. Some of them went on to use heroin.

Maybe that sentence is inartfully worded, but they were certainly using opioids non-medically in that they use

heroin. But not all of them were non-medical prescription opioid users.

Q. Dr. Keyes, your testimony is that you relied on studies that did not involve non-medical use of opioids?

A. Well, they were all heroin users. So in that sense --

MR. FARRELL: Objection, Your Honor, asked and answered. And if he wants to ask about a particular provision in the report, I would ask that he simply show it to the witness.

THE COURT: Yeah. I'll sustain the objection. We need to get through this, Mr. Hester.

BY MR. HESTER:

Q. If you look back at the Muhuri paper that I showed you earlier, Exhibit 2647, that's one involving non-medical pain reliever use; correct?

A. Again, the, the patient populations or those groups overlap, so it's not only non-medical use, although they measured non-medical use.

Q. You're not aware of any studies that have found that people who use prescription opioids only medically have higher rates of heroin use; correct?

A. I do. I am aware of one. It was published after this report.

Q. Which one are you referring to?

A. McCabe 2020.

Q. Let me ask you to look, please, at your deposition testimony out of New York.

A. What was the date of the deposition?

Q. Page -- and McCabe is not disclosed in your report?

A. It was published after the report and after the deposition. But I have knowledge of it and you asked me if I know of any study.

Q. At the time you wrote your report, there were none that had found that people who use prescription opioids only medically have higher rates of heroin use; correct?

A. At the time the report was published, there had not been a study of that. And now there has been.

Q. So the studies that you were looking at involve a transition from prescription opioids to heroin starting with non-medical use?

A. I'm sorry. Say that again.

Q. The studies you were relying on involved a transition from prescription opioids to heroin that started with a misuse of prescription opioids?

A. That's not necessarily the case. As I said before, there's a lot of -- a lot of these studies involve people who started using opioids medically.

Q. And then transitioned to non-medical use; correct?

A. They transitioned to heroin use which is a non-medical use of an opioid.

Q. Let me ask you in relation to your gateway theory, you understand that criminals are responsible for manufacturing illegal opioids like heroin; correct?

A. I have to correct you. It's not a gateway theory. It's not a theory. There's data. So it's a gateway effect.

Q. But you've testified to -- I will ask you more questions about that.

A. Okay.

Q. So in relation to your view that there's a transition from prescription opioids to heroin, I wanted to ask you about the heroin side of that equation. That involves criminal conduct by drug dealers; correct?

A. Yes.

Q. And, so, criminals are responsible for trafficking the illegal drugs that somebody transitions to; correct?

A. As far as I know.

Q. And then in order for the heroin to cause any harm, the end-user actually needs to use it; correct? Needs to use the heroin in order for there to be harm?

A. Yes.

Q. So, so for someone to use an illegal opioid like heroin, there would be at least three crimes committed; right?

A. I, I'm not a legal scholar, so I don't know all the crimes that are committed when someone uses heroin.

Q. But a transition to, to heroin from a prescription opioid would involve criminal conduct in relation to heroin; correct?

MR. FARRELL: Objection, Your Honor, outside the scope of her expertise, calls for a legal conclusion, validation.

THE COURT: Overruled. I think this is proper cross.

THE WITNESS: Can you restate the question?

BY MR. HESTER:

Q. The -- for someone to transition from prescription opioids to heroin, there would have to be illegal acts involving the, the manufacture, sale, and use of the heroin; correct?

A. I would imagine, yes.

Q. I've written on the board, Dr. Keyes, "depends on criminal conduct."

So let's talk a little bit more, Dr. Keyes, about your definition of causation.

First, I want to make sure we're all on the same page about terminology.

When you use the term "cause," you're using that term as it's used by epidemiologists; correct?

A. That's right.

Q. An epidemiologists considers something a cause if it's

a factor that contributes, at least in part, to the development of an illness, at least in some individuals; correct?

A. Yes, something without which the outcome would not have occurred when and how it did is the common definition we use in our classes.

Q. So under the epidemiologist definition of cause that you're applying, the cause need not be temporally proximate to the outcome; correct?

A. That's right.

Q. And it's true that a cause can occur early in life and an intervening cause can occur later in life and those could still be causes for an epidemiologist; correct?

A. Yes.

Q. And there can also be multiple causes for a single event; correct?

A. Yes.

Q. Causes, as you use the term, can be distant in time; correct?

A. Can be?

Q. Distant in time?

A. Yes.

Q. And causes can come before or after one another in a sequence of causes; correct?

A. Yes.

Q. So a cause does not need to be the closest or the most recent cause to be considered a cause by an epidemiologist; correct?

A. That's right.

Q. A cause does not need to be the primary or most important cause to be considered a cause by an epidemiologist; correct?

A. I don't know what you mean by primary or most important.

Q. In other words, there could be multiple causes that might have different weights and they might all be viewed as causes by an epidemiologist; correct?

A. I don't know what you mean by different weights.

Q. Something does not need to be the direct cause to be considered a cause by an epidemiologist, does it?

A. Again, this is not terminology that I'm familiar with. And, so, I'm not sure what's the direct cause.

Q. So, so you don't evaluate the question of direct causes in your work as an epidemiologist?

A. I guess if you could provide the definition of "direct." I mean, we have a definition of "cause" and "causation" that we use when we evaluate the literature.

Q. Let me see if I can get at it another way.

I take it, first, you do recognize that there's an important difference between association and causation;

correct?

A. Causation is a subset of association. They're not different.

Q. So there could be two events or two things that are -- have an association with each other that -- where there's not causation; correct?

A. Yes.

Q. And you could also have some event that happens temporally prior to another event, and the first event is not necessarily the cause of the second; correct?

A. Yes.

Q. So an association means that there's a relationship between two or more variables; correct?

A. Yes, one -- the outcome occurs with greater frequency in the exposed and the unexposed, for example.

Q. And that doesn't necessarily mean that one variable in the association causes the other?

A. It doesn't necessarily mean that.

Q. And, so, in assessing whether an association is causal, you have to account also for other potential causes; correct?

A. That would be a consideration of alternative perspectives in the criteria that I've evaluated.

Q. You're familiar with the concept of multifactorial diseases; correct?

A. I am.
Q. And that's when a single cause does not produce the disease but, rather, the disease is the result of a combination of many causes?
A. More than one.
Q. And is it the case that most diseases are multifactorial?
A. I'm not sure if I would say most, but many diseases are multifactorial.
Q. And OUD is a multifactorial disease; correct?
A. Well, there's one necessary cause, and then there are other potential causes as well.
Q. So when you refer to OUD as, as a multifactorial disease, that means that there's no single cause; there's, there's multiple causes?
A. There's one necessary cause, and then there are other contributing causes.
Q. And when you say one necessary cause, you're meaning there has to be some exposure at some time to an opioid or else you would never develop an OUD?
A. That's right.
Q. But, otherwise, there could be other multiple causes that also contribute to the development of OUD in an individual?
A. Yes.

Q. And it's also true, isn't it, that if you don't know about the other causes of a disease, you may make incorrect causal inferences based on measures of association from epidemiological studies?

A. No, I wouldn't say that that is true across the board. It really depends on the research question that you're looking at. We in epidemiology call it black box epidemiology, for example.

If you do an experiment, you might not know every single contributing cause of the outcome. But as long as the exposure is randomly assigned or that you can control for enough factors that, you know, net of those controls, you can make inference. You don't need to know every single contributing cause. That's the whole kind of basis for epidemiology that we can infer causation from group comparison.

Q. But there are circumstances where if you haven't fully identified other causes, you can make incorrect causal inferences; correct?

A. It would really depend on the specific situation. I can't answer that in the abstract.

Q. Now, Dr. Keyes, there was a heroin problem in the United States well before there was an opioid crisis; correct?

A. There has been heroin prevalent in the United States at

various levels at various times for as long as we've been measuring drugs.

Q. And, and you recall previously we've discussed your allocation of overdose deaths to prescription opioids the way you had done your indirect and direct allocations; right?

A. Yes.

Q. And you attributed 53.4 percent of the illicit opioid deaths indirectly to prescription opioids in your methodology; correct?

A. I don't think it was illicit opioids deaths. It was all overdose deaths.

Q. The -- am I right that you -- your development of deaths that you attributed indirectly due to prescription opioids was based on a figure of 53.4 percent of those deaths being attributed to prescription opioids?

A. Yes, opioid overdose deaths that were not directly attributable to prescriptions.

Q. So for that group, the opioid overdose deaths that were not directly attributed to prescription opioids in your methodology, you used a 53.4 percent figure for that attribution?

A. I did.

Q. And you took that attribution figure, that 53.4 percent, from NSDUH data on the number of heroin users

who reported having used prescription drugs before or at the same time as their first use of heroin; is that correct?

A. That's right.

Q. And you believe that figure was reliable for the use in allocating illegal opioid deaths as a result of your analysis?

A. I do.

Q. Let me ask you to look at another document, please.

MR. HESTER: May I approach, Your Honor?

THE COURT: Yes.

BY MR. HESTER:

Q. Dr. Keyes, we've handed you a document marked as Defendant's West Virginia Exhibit 2579. It's an article written by Theodore Cicero and others, "Increased Use of Heroin as an Initiating Opioid of Abuse: Further Considerations and Policy Implications."

Do you see this document?

A. I do.

Q. And you've seen this document before I take it?

A. I have seen it before.

Q. And who --

A. I don't know that this is on my reference list, but I'm familiar with the paper.

Q. Yes. I think, I think this is not listed on your reference materials, but you do rely on other materials by

Theodore Cicero in your report; correct?

A. Yes. I, I know the paper. I don't think it's on my reference list or on my materials considered list. I just want to make that clear.

Q. What I wanted to ask you about is this statement from -- in this Cicero paper, Page 2. And it's in the right-hand column under the heading "Heroin as an Initiating Opioid."

There's a statement that says, "Heroin use as a first opioid grew sharply from 8.7 percent of the sample in 2005 to almost 31.6 percent in 2015."

Do you see that?

A. I do.

Q. And does that accord with your understanding that heroin use as a first opioid has grown sharply over time and is now roughly around 30 percent?

A. Well, this is a different population than the one that I used for my calculation. So this is a population of people who were, who were -- I'm not so familiar with the methods as I didn't rely on it. But this is part of the SKIP program, the Survey of Key Informant Patients. I don't know what the sample size is. 5,885 people who -- I don't know where they -- adults entering their substance abuse treatment program with a primary diagnosis of opioid use disorder.

Q. And so, so just to be clear on this, so this Cicero study is looking at a population of people who are entering treatment for opioid use disorder?

A. That's what it, it seems to be.

Q. And you're familiar with this paper?

A. I'm generally familiar with the paper.

Q. And, and my question was fairly narrow focusing on this one sentence. Are you aware that there's been an increase in heroin as a first opioid being used by people who are reporting opioid use disorder?

A. This study shows that there has been an increase in heroin use as the first opioid.

Q. And you're not aware of any contrary data in West Virginia, are you?

A. Well, I guess I am in that if you look at the, at the NSDUH data, for example, and other data sources they would show different percentages. I haven't tried to adjudicate between other sources at this point since I didn't rely on the study.

Q. Well, this, this study reflects heroin use as the first opioid rising to over 30 percent by 2015; correct?

A. This study has heroin use as the first opioid -- yes, to 31.6 percent in 2015.

Q. And it's reflecting that that has been increasing; correct?

A. In this sample, that percentage increased.
Q. And does that accord with your general understanding that there has been, there has been an increase in opioid -- in heroin with the opioid first initiation?
A. I have not undertaken that analysis.
Q. The Cicero paper reflects this analysis here; correct?
A. Well, the Cicero paper still shows that over 60 percent of people started with prescription opioids, which is what's in my report. So the 2015 data in Cicero is consistent with my report that 60 percent started with prescription opioids.
Q. Well, but your report talks about 80 percent starting with prescription opioids.
A. The NSDUH number is slightly smaller. So it's within the range of the prevalences that I report. This is, this is very consistent with what other studies have shown.
Q. But the Cicero data does reflect an increase in the percentage of people using heroin as the first opioid; correct?
A. In a -- in the small treatment-seeking sample which does not generalize noise. There are other literature to corroborate it. This sample showed an increase, although prescription opioids remain much more prevalent.
Q. And if you take the Cicero number, it's, it's lower than the 80 percent number that you cited in your report as reflecting prescription opioids as the opioid of first use;

correct?

A. Well, it is within the range of what I report in the report on the proportion of people who began using prescription opioids before heroin.

Q. And just to be clear, the NSDUH data, you reflect nearly half of people reporting that prescription opioids were the opioid of first use; correct?

A. Yes.

Q. Not 80 percent?

A. Yes. And I go into detail in the report on the differences between that number and why I used it versus other numbers that are closer to what Cicero reports of 60 percent starting with prescription opioids.

Q. You don't know whether the percentage of heroin users who started with heroin as their first opioid has increased since 2015, do you?

A. No.

Q. You published 306 peer-review articles I believe you said, Dr. Keyes; is that right?

A. Yes.

Q. And between 35 and 40 of those articles relate specifically to opioid use and related harms; correct?

A. That's right.

Q. And you've never published an article stating that prescription opioid use causes later heroin use; correct?

A. I believe my scientific writings would be consistent with the gateway effect. There's really no debate in the literature on that.

So my articles that have been on prescription opioid use and other related harms due to opioid use, including I think the paper that we talked about earlier today in the Annual Review of Public Health, certainly would reflect that opinion.

Q. You've never, you've never published an article saying -- stating that prescription opioid use causes later heroin use?

A. I don't know that that sentence has ever appeared, but it's certainly in the papers, all the, those opinions that reflect the scientific consensus that is in the articles that I've written on opioid use.

Q. No, but I'm really asking a very narrow question which is have you stated the conclusion that prescription opioid use causes later heroin use? And you have not; correct?

MR. ACKERMAN: Objection, asked and answered.

THE COURT: Overruled.

THE WITNESS: I don't believe that sentence -- I don't know if that sentence has ever appeared in those 35 to 40 articles, but it's possible those combination of words have not.

BY MR. HESTER:

Q. And there's, there's no other article that has stated that conclusion, no public article published by anyone else stating that prescription opioid use causes later heroin use; correct?

A. I would have to disagree with that. I mean, I think the information I've cited in this report consistently shows, including from Nora Volkow and others, that prescription opioids and heroin are pharmacologically similar; that there's a high rate of transition between the two, or higher than people who don't use prescription opioids. And all of that information is consistent in those scientific articles.

You know, scientists in general, and especially epidemiologists, we talk about the data and the evidence. That's what we do in our articles. So I think that that's really clear in the literature.

Q. Dr. Keyes, the reports that you're referring to are ones that state an association between prescription opioid use and misuse and later heroin use; correct?

A. I would have to disagree.

Q. Those are the reports you're referring to?

A. I disagree. I think that the -- what's written in the article, if you look at the Public Health Association report of all the schools of public health, there is consistent language and literature that would, would indicate that

there is a scientific consensus that this is a causal relationship.

Q. And you state -- and you're asserting that that is found in the 16 studies that you've relied on in your report?

A. I'm sorry. That what is found?

Q. Do you, do you assert that the 16 studies you've relied on in your report find causation, find that prescription opioid misuse causes later heroin use?

A. That's not what my testimony was. My testimony is that there is sufficient consensus across the materials that I relied on that this is a causal relationship.

I independently undertook my own analysis of those 16 studies and others and compared it to the frameworks that we use in public health for making decisions about causation.

So I think what we talked about on Friday was that any one study is not sufficient to go from association to causation. But then when you look at the body of literature, that's what, that's what epidemiologists do. And that's what I and others have done that are cited in this report.

Q. But let me stay very narrowly focused on the 16 studies you relied on. And those 16 studies, none of those studies, none of those studies goes beyond finding an association to finding causation between prescription opioid use and later

heroin use?

MR. ACKERMAN: Objection, asked and answered and misstates prior testimony.

THE COURT: I think it has been, Mr. Hester.

MR. HESTER: Let me ask to pull up the New York *Frye* transcript, please, Page 166.

BY MR. HESTER:

Q. So this is the -- let me go back to the first page. So this is the testimony you gave in the *Frye* hearing in September, 2020. Is that right, Dr. Keyes?

A. Yes.

Q. Let me ask you to look at the question and answer at Page 166, lines 3 to 7.

There's a question that was asked you, "Going back to that distinction we drew between causation and association, am I accurate that none of those studies make the step of going beyond association to causation?" That was the question.

And your answer was, "No one study alone, no."

Was that your answer?

A. That's what I just said.

MR. FARRELL: Objection, Your Honor.

THE COURT: Yes.

MR. FARRELL: This isn't impeachment. This is validation of what she testified to.

THE COURT: Well, I know.

I've got the point, Mr. Hester. You're going to have to move along.

MR. HESTER: All right, Your Honor, I'll move it on.

BY MR. HESTER:

Q. On Friday, Dr. Keyes, you testified about a study that Banerjee and colleagues had prepared relating to Veterans Administration data; right?

A. Yes.

Q. And you testified that Banerjee is a protective -- sorry. You testified that Banerjee is a perspective study that follows groups of prescription opioid users and non-users to determine the risk of heroin initiation; right?

A. Yes. I assume there's a copy of the study that I can look at.

Q. Yes. I can get that for you.

MR. HESTER: May I approach, Your Honor?

BY MR. HESTER:

Q. Dr. Keyes, we've handed you what's been marked as Defendants' West Virginia Exhibit 2436, "Non-Medical Use of Prescription Opioids is Associated with Heroin Initiation Among U.S. Veterans."

Do you see that?

A. I do.

Q. And is this the Banerjee article that you were discussing?

A. It is.

Q. And it's headed again -- it's focusing on non-medical use of prescription opioids; correct?

A. Well, again, not exactly. I mean, it's asking about non-medical -- the, the questions that they asked queried non-medical use, but there is quite a bit of overlap, especially in the veteran population, between medical and non-medical use.

Q. And do you understand -- if you look at Page --

MR. FARRELL: Excuse me, Mr. Hester.

MR. HESTER: Yes.

MR. FARRELL: Is this the -- is this the same article that we talked about yesterday?

MR. HESTER: Uh-huh.

BY MR. HESTER:

Q. Am I right, Dr. Keyes -- I understood this was the Banerjee article you had discussed in your testimony on Friday.

A. Look at the Results section because these authors do publish a lot. Yes, I believe it is.

MR. FARRELL: I'm sorry. The format threw me off. I'm sorry. My apologies.

BY MR. HESTER:

Q. And do you see at the top of Page 3 of this article, Dr. Keyes, it refers to people who engage in non-medical use of prescription opioids may be at higher risk for transition to heroin use? Do you see that, first line?

A. Yes. It says, "Persons who engage in non-medical use of prescription opioids may be at higher risk for transitioning to heroin use in part because heroin has become more accessible and less expensive than prescription opioids in many U.S. settings."

Q. Does that accord with your understanding?

A. Yes.

Q. And, so, this is talking about persons who are engaged in non-medical use of prescription opioids; right?

A. Well, not non-medical only. So it leads to non-medical use.

Q. But they have to be engaged in some non-medical use to be part of this analysis; correct?

A. To be a part of the exposed group. There's also an unexposed group who did not use prescription opioids.

Q. And, so, this -- the study population that they were looking at, if you look at Page 2, was a group of HIV infected and uninfected veterans; is that right?

A. Yes.

Q. And approximately 45 percent of the participants in

this study were HIV infected; right?

A. That's right.

Q. And the authors go on to -- if you look at Page 8, the authors state -- if you look at the bottom paragraph -- that the study enrolled individuals who are likely at higher risk for heroin initiation than the general veteran population.

Do you see that?

A. Yes.

Q. And does that accord with your understanding?

A. Yes. That's why we use a broad range of studies to draw conclusions from in the literature.

Q. And it also goes on at Page 9, the last sentence, next to the last sentence of the article. It says -- states that the demographics of a veteran population are substantially different from young college students.

Do you see that?

A. Yes.

Q. And does that also accord with your understanding?

A. That college students are a different demographic than middle-aged veterans?

Q. The veterans being studied in this report.

A. Yes.

Q. And then if you look at Page 4 of this document, the study -- the survey that was being measured was looking at persons who used prescription opioids non-medically either

prior to or concurrent with initiation of heroin use; is that right?

A. I'm sorry. What sentence are you --

Q. If you look at -- if you look in the middle of the page, the end of the paragraph under "Measures," they refer to new onset, NMUPO, was considered to occur prior to or concurrently with heroin initiation.

Do you see that?

A. Yes.

Q. And, so, do you understand that this study was looking at persons who had either engaged in non-medical prescription opioid use before or concurrently with use of heroin?

A. Well, it just -- I think the word "concurrently" they're using here is in the same year.

Q. Right. So there could be heroin use and non-medical use of prescription opioids in the same year and those would be defined as concurrent use under the study; right?

A. That's right.

Q. So the authors' findings are not limited to people whose non-medical prescription opioid use preceded heroin initiation; correct?

A. By and large, the vast majority of the people in the study who are in the risk group, they're looking at -- if I could explain survival analysis for a moment.

The way survival analysis works, which is on Figure 2, which is that you're measuring time from exposure to outcome.

So the people who had prescription opioid use and heroin use in the same year, their time to outcome is going to be very, very short. So in Figure 2 they're going to be part of that first bar of the time series graph.

And you can look at the time series graph and see the blue line and the red line. And the red line is incident NMUPO prior to or concurrent to heroin initiation, and then the amount of time that has passed to their heroin initiation.

So by far, what this study shows is that the people who are using in the same year are not contributing to that five times risk number that is in Table 2, I think it is, that I spoke about on Friday.

Q. But --

A. Because, because of the way time series works, you measure that -- the, the hazard of initiation is measured as a factor of time.

Q. But the sample that this study is looking at includes people who would initiate both heroin and non-medical use; correct?

A. They didn't exclude those people, but the five times risk number is not going to incorporate. They're largely

uninformative. If you're trying to -- if you can kind of consider whether -- you know, you want to know what the risk of heroin initiation is after you use prescription opioids. So people who used in the same year are not contributing a lot to that person time.

Q. Let me ask you about another document you discussed in your examination on Friday. You discussed a report that was put out by the Association of Schools and Programs of Public Health; correct?

A. Yes.

Q. And you described that report as a consensus statement of the schools; is that right?

A. Yes.

Q. Let me ask you to look at that paper for a minute, please.

MR. HESTER: May I approach, Your Honor?

THE COURT: Yes.

BY MR. HESTER:

Q. Dr. Keyes, we've handed you what's been marked as Plaintiffs' Exhibit 43124. It's entitled "Bringing Science to Bear on Opioids."

Do you see that?

A. Yes.

Q. And this is the report you were talking about in your examination on Friday; is that right?

A. That's right.

Q. And this is not an epidemiological study; correct?

A. It's a review of the literature which I would consider to be an epidemiological study.

Q. It's a report of a task force of this Association of Schools and Programs of Public Health; correct?

A. Yes. But contained in it is reviews of the literature.

Q. But it's a task force report. It doesn't purport to be a consensus statement of all the schools in this association; correct?

A. I believe on Page 3 that's what it says.

Q. But this is a task force report that was then circulated by the Association of Schools and Programs?

A. You know, the ASPPH Board of Directors has reviewed and endorsed the report.

Q. But it was prepared by a task force, not by a group of schools; correct?

MR. ACKERMAN: Your Honor, asked and answered, objection.

THE COURT: Sustained.

BY MR. HESTER:

Q. The -- let me ask you to look at the authors of the report, please. If you look at the task force members --

A. What page is that?

Q. It is Page 39 using the small numbers in the bottom right. Do you see these are the members of the task force?

A. Yes.

Q. And is it your understanding that these are the folks who prepared the report?

A. Let's see. Not exactly. On Page 3 it says, "After much deliberation and extensive review of the scientific literature, consultation with other experts, and the practical experience of task force members."

Q. So --

A. So I would say that these are some of the people that were centrally involved in the development of this document certainly, but that it's not exclusively this group.

Q. Right. Okay. So these -- the listing here on Page 39 that we're looking at would reflect people who were centrally involved in the task force report?

A. That would be my assumption.

Q. And do you know that Judith Feinberg listed here is an expert witness in this case?

A. I'm not familiar with all of the other experts in the case.

Q. Do you know that she is an expert witness in this case?

A. I heard her name this week when I was -- but I haven't read her report.

Q. Do you know that Andrew Kolodny is an expert witness in

this case, another person listed in this membership of the task force?

A. No.

Q. You don't know if he's an expert in this case?

A. I didn't know that. I know he has a lot of expertise in opioid policy.

Q. Do you know he's an expert witness in other opioid litigation?

A. I, I, I've heard his name referenced. I mean, he's an expert on opioid use. It seems reasonable that he would be --

Q. I was really asking about whether he's testifying as an expert in this litigation.

A. I've heard his name in other litigation.

Q. Do you know -- do you see Caleb Banta-Green who's also listed as one of the members of this task force?

A. Do I know him?

Q. Do you see his name listed there?

A. Yes.

Q. And do you know that he's at the University of Washington and is an employee of the State of Washington?

A. That's what it says.

Q. And do you know that Washington State is suing these defendants?

A. My understanding was that many states are suing.

Q. But Washington State, do you know that?

A. I'm not aware of every lawsuit.

Q. Do you see Brendan Saloner is also listed here in this task force membership?

A. I see that.

Q. And if you look, if you look a few pages back at Page 47, there's a disclosure of conflict of interest issues. And the last bullet on the page is, "Dr. Brendan Saloner reported that he has a nondisclosure agreement with Monument Analytics, a litigation consulting research firm run by a colleague (Caleb Alexander)."

Do you see that?

A. Page 47?

Q. Yes.

A. Yes, I see that.

Q. And do you see that description of Dr. Saloner?

A. I see that description of Dr. Saloner.

Q. And are you aware -- it reflects here that he's a colleague of Caleb Alexander. Do you see that?

A. Yes.

Q. And are you aware that Dr. Alexander is an expert witness in this case?

A. I am.

Q. Let's turn back to the Muhuri study if we could. And I wanted to go back, wanted to go back to your statement about

the 80 percent number, the 80 percent number being people engaged in non-medical use of prescription opioids prior to heroin transition. Do you recall that?

A. I do.

Q. And Muhuri is one of the papers you cite for that proposition; right?

A. It is one, yes.

Q. So let's look, if you could, at Page 11 of this document, please. And Table 3 here reports that percentage of people who started using heroin based on different factors that they present; correct?

A. Yes.

Q. And the last six rows on Page 11 give us data on the percentage of heroin users with and without prior non-medical pain reliever use; correct?

A. That's right.

Q. And, so, if we look over at the right-hand side we can see this number of 79.5 percent; correct?

A. Yes.

Q. And that's the number that you cite prior -- non-medical prescription use prior to heroin initiation; is that right?

A. That's right.

Q. And do you see also it states, if you look a little bit further down, that it also indicates that -- how many of

these same individuals have prior illicit drug use before their use of non-medical prescription opioids; correct?

A. Yes.

Q. And it reflects that 79.5 percent of persons engaged in non-medical prescription use had prior use of illicit drugs; correct?

A. Yes.

Q. So that's the same percentage as the percentage that goes on to heroin; correct?

A. That's right.

Q. And if you look --

A. Well, it's not the percentage that goes on to heroin. It's the percentage of heroin users who use non-medically first.

Q. So the percentage -- 79.5 is the percentage of people who engaged in non-medical use and then subsequently were using heroin based on the Muhuri study; correct?

A. It's the proportion of heroin users who started opioid use with prescription opioids.

Q. And, and this study also reflects that that same proportion, that same 79.5 percent, had also used other illegal substances before their use of non-medical prescription opioids; right?

A. That's right.

Q. And if you look over on the next page, it defines the

illicit drugs that are referred to there. And it says, if you look at Footnote 2, illicit drugs include marijuana, hashish, cocaine, including crack, hallucinogens, and inhalants. Do you see that?

A. I do.

Q. So according to this Table 3, every single heroin user that had prior non-medical pain relieving use also had prior illicit drug use; correct?

A. That's right.

Q. So prescription opioids were not the only drug of abuse for any of the individuals who used prescription opioids non-medically and then subsequently used heroin; correct?

A. Well, we only know from this not what their drugs of abuse are, but that they had prior use of marijuana and other drugs.

Q. So they had other -- they had abused other drugs before their non-medical use of prescription opioids; correct?

A. I don't know that we know that they were before the non-medical use of prescription opioids, but they did have prior other illegal drug use like marijuana.

Q. And according to Table 3, nearly all of the heroin users who did not have prior non-medical pain reliever use had prior illicit drug use; is that correct?

A. Yes. Among those who -- with no prior non-medical pain reliever use, 19.4 percent of the 20.5 percent had also used

another illegal drug.

Q. So if we add those two together, in this study 98.9 percent of the heroin users previously used illegal drugs like marijuana, hashish, cocaine, crack, hallucinogens, and inhalants; is that right?

A. That's right.

Q. So I'm going to put another entry on the board here. What I've written there is "other substance abuse" to reflect this finding of Muhuri.

A. Well, substance abuse is a DSM category. What this study reflects is that they had other substance use.

Q. Other substance use of illegal drugs?

A. Other substance use of an illegal drug.

Q. So if I change that to "other substance use of illegal drugs" is that more accurate?

A. Yes.

Q. And as a more general proposition, it's true, Dr. Keyes, that a majority of heroin users started using marijuana or cocaine or other illegal drugs before they turned to heroin; correct?

A. Among heroin users, the most common first substance use is tobacco and alcohol. And there is then a progression to other drugs as well. But the, the timing of those vis-à-vis prescription opioid use is quite variable.

Q. But --

A. Most people who use heroin have used alcohol and tobacco. And then there are other drugs that are used as well. But the timing of those is, is variable across studies.

Q. But it's fair to say that a majority of heroin users started using marijuana or cocaine or other illegal drugs before turning to heroin; correct?

A. Yes, that is correct. It's the timing vis-à-vis prescription opioids that is, I think, more relevant.

Q. But you could have a circumstance where persons who used heroin began by abusing another drug like cocaine or marijuana and then used prescription opioids, then used --

A. In this circumstance, because of the pharmacological similarity between prescription opioid use and heroin use, it's a much tighter connection in terms of that transition because oftentimes people who don't have access to prescription opioids, that becomes a catalyst for that transition as drugs become less accessible and more expensive.

Q. I take it, though, that you could have -- and you have observed this sequence of events where persons who use heroin began their abuse of illegal drugs with something like cocaine or marijuana or methamphetamine. Then they may have used prescription opioids, misused prescription opioids, then later used heroin. Correct? That's a

sequence you've seen?

A. I only reviewed the aggregate data. And by far, the biggest risk factor is prescription opioid use. Certainly, I'm sure there is a person in the world who used cocaine before heroin.

Q. Well, I was really asking another question which was you're aware that many of the persons who used heroin after misusing prescription opioids also had previously abused other drugs?

A. I think what these data show is that there's previous use of other drugs.

Q. And when you say other drugs, you're meaning marijuana, cocaine, methamphetamine, et cetera; correct?

A. There is co-occurring use of other drugs. And alcohol and tobacco, I think, would be appropriate to add to that list as well. But the closest connection in the transition to heroin is the exposure to prescription opioids.

Q. It's also true -- I think you said this before -- that a majority of heroin users have used alcohol before they started using heroin?

A. Used alcohol.

Q. How about abused?

A. I haven't done a recent search of the literature for that. But certainly in terms of alcohol use, the vast majority of people who have used heroin have used alcohol.

MR. HESTER: Let me pull up the New York *Frye* transcript, please, Page 188, lines 3 to 10.

BY MR. HESTER:

Q. Dr. Keyes, I take it you recall testifying in this *Frye* hearing in New York?

A. Yes.

Q. And the question was, "Do you know what percentage of people who have used heroin abused alcohol before using heroin?"

And you said, "Abused alcohol? Do you mean have alcohol use disorder?"

And the question was, "Or abused it in some way, used it excessively in some way."

And your answer was, "It's a majority."

Do you see that?

A. Yes.

Q. And was your answer correct when you gave it?

A. And that's what I just said. They used alcohol, not alcohol use disorder, which is the distinction I was trying to make. So that's consistent.

Q. But the question was abused it in some way or used it excessively. And that's --

A. Used excessively is very different than having an alcohol use disorder.

Q. Your own research has shown that past-year drug use,

other than non-medical use of prescription opioids and alcohol use disorder, are the strongest factors associated with non-medical use --

A. I'm sorry. Can you say the question again?

Q. Yes, sorry. Your own research has shown that past-year drug use, other than non-medical use of prescription opioids and alcohol use disorder, are the strongest factors associated with non-medical use of prescription opioids. Correct?

A. You said past -- I'm sorry. I don't think the question quite -- unless I'm misunderstanding and it's the end of the day, but I think you just said using drugs other than prescription opioids is the strongest risk factor for using prescription opioids other than -- it's a little bit tautological the way that it's phrased.

Q. Fair enough. Let me see if I can ask it again.

Is it correct, Dr. Keyes, that past-year drug use is the strongest factor associated with non-medical use of prescription opioids?

A. Strongest compared to what?

Q. Strongest risk factor for incidence of non-medical use of prescription opioids.

A. Exposure to opioids is the strongest risk factor. There's a study that is potentially being taken out of context. I'm sure we can look at it.

MR. HESTER: Let me pull up the New York *Frye* hearing, please, 188, lines 3 to 8.

BY MR. HESTER:

Q. The question was asked, Dr. Keyes, "Am I right that your own research has shown that past-year drug use --"

A. That's not what's shown on here.

Q. Sorry.

MR. HESTER: 188, lines 3 to 8, please. No. Sorry. Lines 13 to 18. Apologies.

BY MR. HESTER:

Q. Okay. Am I right that -- the question was, Dr. Keyes, "Am I right that your own research has shown that past-year drug use, other than non-medical use of prescription opioids and alcohol use disorder, are the strongest factors associated with non-medical use of prescription opioids?"

And your answer was, "Yes."

Correct?

A. Yes.

Q. And was that answer accurate when you gave it?

A. Yes, in the context of the other questions that had positioned what those other factors we were comparing that to was. We can't compare it to the universe of all risk factors.

Q. That's a generally accepted view in the epidemiological

community as you expressed here on the screen; correct?

A. Again, you have to start with a list of the risk -- if you're going to say this is the strongest risk factor, you have to start with the list of risk factors you're assessing.

The strongest risk factor for non-medical prescription opioid use is exposure to opioids. If you're talking about a different list of risk factors, drug use is certainly correlated with non-medical use of prescription opioids, of course. But you have -- to say what the strongest is, you need some ranking.

MR. HESTER: Your Honor, I'm ready to go to another document but --

THE COURT: Well, let's quit until in the morning, Mr. Hester. I hope you can wrap this up pretty soon.

MR. HESTER: I will, Your Honor.

THE COURT: I've given you the whole day today and we need to get this case moving.

MR. HESTER: Yes, Your Honor. And maybe if I can -- I understand, first of all, what the Court is saying. I will undertake to do that. If I can just give a bit of perspective that we feel this is a very important piece of --

THE COURT: Well, I understand that.

MR. HESTER: -- testimony and we felt we needed to

explain some of the methodologies. But I, I don't mean to burn the Court's time and I'm not trying to. We'll be as efficient as we can be.

THE COURT: Okay. Mr. Majestro has appeared in the courtroom and --

MR. MAJESTRO: Your Honor, I just wanted to inquire of the defendants. I don't want to beat a dead horse, but we inquired Friday and we were told a little bit after lunch to finish this cross-examination, verified that over the weekend.

We've got a witness in from California who we thought we were going to put in tomorrow. We've had a witness who we were ready to put on this afternoon. We're starting to stack them up.

I mean, it basically -- we agree this is an important witness, but basically three-to-one cross-examination and direct appears to us to be a bit on the excessive side.

THE COURT: Well, I'm getting very concerned about us not getting things done here. And I realize this is an extremely important witness and these are important points, but at some point we've got to get this story told.

MR. MAJESTRO: Your Honor, may I inquire of Mr. Hester how much time he has -- thinks he has left and whether any of the other defendants are going to be cross-examining so we can plan our witnesses?

MR. HESTER: Well, Your Honor, first of all, I'm not sure that there was a representation made on Friday that we were going to finish in X amount of time.

THE COURT: Well, are there -- will there be other cross-examinations of this witness?

MS. MCCLURE: I am not cross-examining this witness, Your Honor.

THE COURT: How about you, Ms. Hardin?

MS. HARDIN: There is a possibility that I would have about a handful of questions, but I would like to have the opportunity to consult with Mr. Hester before making any final determinations about that.

THE COURT: Okay. Well, let's -- I understand everybody's concerns and I don't have a ready answer for any of this at 5:00 on Monday afternoon. So we'll reconvene at 9:00 in the morning and see where we are then.

MR. HESTER: And, Your Honor, I will undertake overnight to look hard and make sure I'm tight in the morning.

THE COURT: Thank you.

MR. MAJESTRO: If you could get us some estimate as soon as you feel you're in a position to do so, that would be helpful for planning purposes. We appreciate it.

THE COURT: Okay. We'll see everybody at 9:00.

(Trial recessed at 5:04 p.m.)

CERTIFICATION:

I, Ayme A. Cochran, Official Court Reporter, and I, Lisa A. Cook, Official Court Reporter, certify that the foregoing is a correct transcript from the record of proceedings in the matter of The City of Huntington, et al., Plaintiffs vs. AmerisourceBergen Drug Corporation, et al., Defendants, Civil Action No. 3:17-cv-01362 and Civil Action No. 3:17-cv-01665, as reported on June 14, 2021.

S\Ayme A. Cochran
Reporter

s\Lisa A. Cook
Reporter

June 14, 2021
Date

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